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Search Notes

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FILE LAST UPDATED: 11 Aug 2004  (20040811/ED)

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L78  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:674642  HCAPLUS
DN   137:210939
ED   Entered STN:  06 Sep 2002
TI   Methods of use of compounds which inhibit the stem cell
     factor signaling pathway
IN   Longley, B. Jack
PA   USA
SO   U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 306,143.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  C12Q001-00
NCL  435004000
CC   1-7 (Pharmacology)
     Section cross-reference(s): 2
FAN.CNT 2
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   US 2002123031        A1    20020905    US 1999-474478          19991229 <--
     US 6576812           B1    20030610    US 1999-306143          19990506 <--
     WO 2000067794        A1    20001116    WO 2000-US12405         20000505 <--
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-306143       A2    19990506  <--
     US 1999-474478       A2    19991229
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 2002123031    ICM    C12Q001-00
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NCL 435004000
US 2002123031 ECLA C07K016/28A <--
US 6576812 ECLA C07K016/28A <--

AB The invention provides a method of preventing or treating in a subject **contact dermatitis** which comprises administering to the subject an amount of a compound capable of inhibiting the **stem cell factor signaling pathway** effective to prevent or treat **contact dermatitis** so as to thereby prevent or treat **contact dermatitis** in the subject. The invention also provides a methods of preventing or treating in a subject **hyperpigmentation**, **asthma**, **cutaneous inflammation**, anaphylaxis and **bronchospasm**, **mastocytosis**, **tumors** which express activated **kit**, and conception.

ST **stem cell factor signaling pathway** inhibitor therapeutic; **dermatitis hyperpigmentation asthma stem cell factor signaling pathway** inhibitor; **skin inflammation mastocytosis stem cell factor signaling pathway** inhibitor; anaphylaxis **bronchospasm tumor stem cell factor signaling pathway** inhibitor; contraceptive **stem cell factor signaling pathway** inhibitor

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgA; **stem cell factor signaling pathway** inhibitors for)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgD; **stem cell factor signaling pathway** inhibitors for)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgE; **stem cell factor signaling pathway** inhibitors for)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgG; **stem cell factor signaling pathway** inhibitors for)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IgM; **stem cell factor signaling pathway** inhibitors for)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**SCF**-cleaving; **stem cell factor signaling pathway** inhibitors for)

IT Drug delivery systems
(anal; **stem cell factor signaling pathway** inhibitors for)

IT Ligands
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding; **stem cell factor signaling pathway** inhibitors for)

IT **Dermatitis**
(**contact**; **stem cell factor signaling pathway** inhibitors for)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion products; **stem cell factor signaling pathway** inhibitors for)
IT Digestive tract, **neoplasm**
(gastrointestinal stromal **tumor**, inhibitors; **stem cell factor signaling pathway** inhibitors for)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized; **stem cell factor signaling pathway** inhibitors for)
IT **Skin, disease**
(**hyperpigmentation**; **stem cell factor signaling pathway** inhibitors for)
IT **Allergy**
(**hypersensitivity**; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(injections, i.m.; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(injections, i.p.; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(injections, i.v.; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(injections, s.c.; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(intestinal; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(intralesional; **stem cell factor signaling pathway** inhibitors for)
IT **Skin**
(keratinocyte; **stem cell factor signaling pathway** inhibitors for)
IT Dimerization
(**kit**; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(liposomes; **stem cell factor signaling pathway** inhibitors for)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(mucosal; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(nasal; **stem cell factor signaling pathway** inhibitors for)
IT Gamete and Germ cell
(**neoplasm**, inhibitors; **stem cell factor signaling pathway** inhibitors for)
IT **Mast cell**
(**neoplasm, mastocytoma**; **stem cell**

factor signaling pathway inhibitors for)
IT Drug delivery systems
(ophthalmic; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(oral; **stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(otic; **stem cell factor signaling pathway** inhibitors for)
IT **Bronchi, disease**
(**spasm; stem cell factor signaling pathway** inhibitors for)
IT Allergy inhibitors
Anaphylaxis
Anti-inflammatory agents
Antiasthmatics
Antitumor agents
Asthma
Canis familiaris
Contraceptives
Dermatitis
Felis catus
Human
Mast cell
Melanocyte
Neoplasm
Peptidomimetics
Signal transduction, biological
Transformation, genetic
Urticaria
(**stem cell factor signaling pathway** inhibitors for)
IT **Stem cell factor**
Transgene
c-**Kit** (protein)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**stem cell factor signaling pathway** inhibitors for)
IT Antibodies and Immunoglobulins
Nucleic acids
Organic compounds, biological studies
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stem cell factor signaling pathway** inhibitors for)
IT Drug delivery systems
(topical; **stem cell factor signaling pathway** inhibitors for)
IT 9004-06-2, Elastase 97501-92-3, Chymase 138359-29-2, **Kit** tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**stem cell factor signaling pathway** inhibitors for)
IT 454746-24-8 454746-25-9 454746-26-0 454746-27-1
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods of use of compds. which inhibit the **stem cell factor signaling pathway**)

L78 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:814345 HCAPLUS

DN 133:361913
ED Entered STN: 21 Nov 2000
TI Methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**
IN **Longley, B. Jack**
PA The Trustees of Columbia University In the City of New York, USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-395
ICS C07K016-00; C12Q001-70
CC 15-3 (Immunochemistry)
Section cross-reference(s): 2, 8, 62, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000067794	A1	20001116	WO 2000-US12405	20000505 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6576812	B1	20030610	US 1999-306143	19990506 <--
	US 2002123031	A1	20020905	US 1999-474478	19991229 <--
PRAI	US 1999-306143	A2	19990506 <--		
	US 1999-474478	A2	19991229		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000067794	ICM	A61K039-395
	ICS	C07K016-00; C12Q001-70
US 6576812	ECLA	C07K016/28A <--
US 2002123031	ECLA	C07K016/28A <--

AB This invention provides a method of preventing or treating in a subject **contact dermatitis** which comprises administering to the subject an amount of a compound capable of inhibiting the **stem cell factor signaling pathway** effective to prevent or treat **contact dermatitis** so as to thereby prevent or treat **contact dermatitis** in the subject. This invention also provides a method of preventing or treating in a subject **hyperpigmentation**, **asthma**, **cutaneous inflammation**, anaphylaxis and **bronchospasm**, **mastocytosis**, **tumors** which express activated **kit**, and conception.

ST **contact dermatitis antiasthmatic** antiallergic monoclonal ACK2

IT Keratins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(14, promoter of gene encoding; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(A, anti-**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Immunoglobulins

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(D, anti-**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(E, anti-**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(G, anti-**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(M, anti-**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Drug delivery systems
(anal; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Dermatitis**
(**contact**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Fats and Glyceridic oils, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(croton; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Bladder
(cystitis, interstitial; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Skin**
(**epidermis**, interadnexal; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Neoplasm**
(gastrointestinal stroma; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Skin, disease**
(**hyperpigmentation**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Allergy**
(**hypersensitivity**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Skin, disease**
(hypopigmentation; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Drug delivery systems
(i.p.; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT **Respiratory tract**
(**inflammation**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Drug delivery systems
(injections, i.m.; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)

IT Drug delivery systems
(injections, i.v.; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(injections, s.c.; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(intestinal; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(intralesional; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(intravesicular; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Abdomen
Ear
(irritant application to murine; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**kit**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(liposomes; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Mast cell
(mastocytoma; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Allergy inhibitors
Anaphylaxis
Antiasthmatics
Asthma
Canidae
Carcinoma
Cat (Felis catus)
Contraceptives
Cosmetics
Dermatitis
Electron microscopy
Mammal (Mammalia)
Melanoma
Molecular weight distribution
Peptidomimetics
Signal transduction, biological
Sunburn
Urticaria
(methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Antibodies
Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Transgene
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(mice bearing; methods for inhibiting **cutaneous**

inflammation and **hyperpigmentation**)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monoclonal, anti-**kit**, ACK2; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**
)
IT Drug delivery systems
(nasal; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Gamete and Germ cell
(**neoplasm**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Promoter (genetic element)
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(of cytokeratin 14 gene; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(ophthalmic; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(oral; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(otic; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(parenterals; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT **Nose**
(**rhinitis**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT **Stem cell factor**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**signaling pathway**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**
)
IT UV radiation
(**skin** injury from; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Olive oil
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT **Bronchi**
(**spasm**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Digestive tract
(stromal **tumor**; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(topical; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Mouse
(transgenic; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT Drug delivery systems
(transmucosal; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT 9004-06-2, Elastase 97501-92-3, Chymase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT 70-34-8, Dinitrofluorobenzene
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
IT 67-64-1, Acetone, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; methods for inhibiting **cutaneous inflammation** and **hyperpigmentation**)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bennett; US 5997865 A 1999 HCAPLUS
(2) Brownell; US 5911988 A 1999 HCAPLUS
(3) Ravetch; US 5877396 A 1999 HCAPLUS

L78 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:64924** HCAPLUS
DN **132:320348**
ED Entered STN: 27 Jan 2000
TI Coexpression of c-**kit** and **stem cell factor** in breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors
AU Hines, Susan J.; Litz, Julie S.; Krystal, Geoffrey W.
CS Department of Medicine, Medical College of Virginia and McGuire VA Medical Center, Richmond, VA, USA
SO Breast Cancer Research and Treatment (**1999**), 58(1), 1-10
CODEN: BCTRD6; ISSN: 0167-6806
PB Kluwer Academic Publishers
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB **Kit**, a tyrosine kinase growth **factor** receptor, and its ligand, **stem cell factor** (**SCF**), are commonly coexpressed in breast **cancer.** We have previously shown that MCF7 cells (that naturally express **SCF**) transfected with a c-**kit** expression vector exhibit enhanced growth in serum-free medium supplemented with IGF-1. Consequently, we wished to examine the interaction of **Kit/SCF** with addnl. growth **factors** important in the biol. of breast **cancer.** MCF7 transfectants expressing **Kit**, cultured in serum-free medium supplemented with EGF, displayed more than twice the growth of controls at identical EGF concns. Similar responses were seen in the presence of heregulin α. The specificity of the **Kit**-mediated response was illustrated by a reduction in heregulin-stimulated growth in the presence of a monoclonal antibody directed against the **Kit** receptor. In addition, EGF-and heregulin-stimulated growth of the ZR75-1 cell line that naturally coexpresses **Kit** and **SCF** was also inhibited by the **Kit** blocking antibody. Preliminary investigations into the **signal** transduction **pathways** activated by these growth **factors** revealed that **SCF** activated both the Ras-MAP kinase and phosphatidyl-inositol-3-kinase (P13 kinase) **pathway.** Both EGF and heregulin activated MAPK but to a lesser degree than **SCF**, and combination of **SCF** with these growth **factors** resulted in enhanced MAPK activation. Assessment of P13K **pathway** activation using anti-phospho-Akt antibodies revealed that EGF was a poor activator of Akt; activation of this **pathway** was markedly enhanced by the addition of **SCF.**

Heregulin activated Akt and addition of **SCF** provided no further activation. Taken together these results suggest that coexpression of **SCF** and **Kit** may enhance responsiveness to erbB ligands by enhancing activation of the MAPK and P13K **pathways.**

ST ckit **stem cell factor** breast **cancer** EGF MAP kinase

IT Cell proliferation
(c-**kit** and **stem cell factor** coexpression in human breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

IT **Stem cell factor**
c-**Kit** (protein)
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(c-**kit** and **stem cell factor** coexpression in human breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

IT Mammary gland
(**neoplasm**; c-**kit** and **stem cell factor** coexpression in human breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

IT Heregulins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α; c- **kit** and **stem cell factor** in breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

IT 62229-50-9, EGF
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(c-**kit** and **stem cell factor** coexpression in human breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

IT 115926-52-8, Phosphatidyl-inositol-3-kinase 142243-02-5, MAP kinase 148640-14-6, Akt kinase 149147-12-6, Akt kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-**kit** and **stem cell factor** in breast **cancer** results in enhanced sensitivity to members of the EGF family of growth factors)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L78 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:780242** HCAPLUS
DN **132:217164**
ED Entered STN: 09 Dec 1999
TI **Stem cell factor**/c-**kit** system in spermatogenesis
AU Mauduit, Claire; Hamamah, Samir; Benahmed, Mohamed
CS INSERM U407, INSERM U407, Faculte de Medecine Lyon-Sud, Oullins, F-69921, Fr.
SO Human Reproduction Update (**1999**), 5(5), 535-545
CODEN: HRUPF8; ISSN: 1355-4786
PB Oxford University Press
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 14
AB A review, with 92 refs., reporting a large number of data, obtained essentially in animal models, that suggest an important role for the **SCF**/c-**kit** system in spermatogenesis and, as a corollary, its potential involvement in spermatogenic defects. One of the major unresolved questions with male infertility is the identification of the mol. origin of a great majority of the spermatogenetic arrests currently diagnosed as idiopathic male infertility. During the past years, several families of regulating factors have been implicated in spermatogenesis defects observed essentially in animal models. Among these factors are **signalling** mols., and particularly the **stem cell factor** (**SCF**)/c-**kit** system. The **SCF** and its receptor c-**kit** are an appropriate example to illustrate the role of **signalling** mols. in the physiol. and pathol. of spermatogenesis. The **SCF**/c-**kit** regulates primordial germ cell migration, proliferation and apoptosis during fetal gonadal development. The **SCF**/c-**kit** also regulates spermatogonia proliferation in the adult animal. In mutant mice, abnormalities of the **SCF**/c-**kit** gene expression, such as gene deletion, point mutation, alternative splicing defect, lead to different types of spermatogenesis alterations (e.g., decrease in primordial germ cell migration, decrease in spermatogonia proliferation). More recently, defects in **SCF**/c-**kit** gene expression

have also been shown in human testicular dysfunctions. Indeed, a reduction in **SCF**/c-**kit** expression has been evidenced in oligozoospermia/azoospermia associated with an increase in the germ cell apoptosis process. In addition, c-**kit** seems to be a good marker of seminoma testicular **tumors**.

ST review **stem cell factor** c **kit** protein spermatogenesis; male infertility **stem cell factor** c **kit** protein review; seminoma **stem cell factor** c **kit** protein review

IT Embryo, animal
(fetus, development; **stem cell factor**/c-**kit** system in spermatogenesis in relation to)

IT **Fertility**
(male, disorder; **stem cell factor**/c-**kit** system in spermatogenesis in relation to)

IT Testis, **neoplasm**
(seminoma; **stem cell factor**/c-**kit** system in spermatogenesis in relation to)

IT **Spermatogenesis**
Testis
(**stem cell factor**/c-**kit** system in spermatogenesis)

IT **Stem cell factor**
c-**Kit** (protein)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**stem cell factor**/c-**kit** system in spermatogenesis)

IT Apoptosis
Cell migration
Cell proliferation
Signal transduction, biological
Testis, disease
(**stem cell factor**/c-**kit** system in spermatogenesis in relation to)

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L78 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:763362** HCAPLUS
DN **132:76859**
ED Entered STN: 03 Dec 1999
TI Regulation of the melanoma cell adhesion molecule gene in melanoma: modulation of mRNA synthesis by cyclic adenosine monophosphate, phorbol ester, and **stem cell factor/ c-kit signaling**
AU Karlen, Stephane; Braathen, Lasse R.
CS Dermatological Clinic, University of Bern, Bern, Switz.
SO Journal of Investigative Dermatology (**1999**), 113(5), 711-719
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell Science, Inc.
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3
AB The melanoma cell adhesion mol. was identified as a human melanoma-associated antigen that increases in expression as **tumors** increase in thickness and begin to acquire **metastatic** potential. Clin. and exptl. evidences suggest that the development of **metastatic** capacity might be the consequence of increased melanoma cell adhesion mol. expression. The mechanisms for upregulation of the melanoma cell adhesion mol. during melanoma progression are, however, still poorly understood. In this study, we show that melanoma cell adhesion mol. expression is tightly regulated at the transcriptional level. Using a combination of CAT reporter assays and semiquant. RT-PCR, we observed that cAMP significantly increases transcription of the melanoma cell adhesion mol. in **nonmetastatic** melanoma cells. In **metastatic** cells, transcription of the gene was constitutive and could not be further increased by cAMP. On the other hand, melanoma cell adhesion mol. promoter activity was impeded upon treatment with phorbol esters or in the presence of **stem cell factor**, a phenomenon which was protein kinase C-dependent. Promoter-deletion studies demonstrated that the first 196 nt of the melanoma cell adhesion mol. promoter region are sufficient to get full expression in **metastatic** melanoma cells. This fragment contains five binding sites for the transcription factor Sp1 and DNA mobility shift expts. showed direct binding of Sp1 to the promoter. In conclusion, our results indicate that Sp1 is sufficient to drive constitutive melanoma cell adhesion mol. expression in **metastatic** melanoma cells. In **nonmetastatic** cells, however, melanoma cell adhesion mol. expression is repressed and we speculate that **stem cell factor/ c-Kit signaling** might be responsible for the control of melanoma cell adhesion mol. synthesis, and thus, perhaps, of melanoma progression and metastasis.
ST melanoma cell adhesion mol gene regulation; cAMP **stem cell factor** MCAM mRNA melanoma
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MCAM (melanoma cell adhesion mol.); regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)

IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(MCAM; regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Sp1; regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT Transcriptional regulation
(activation; regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT Melanoma
(metastasis; regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT Melanoma
Signal transduction, biological
(regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT **Stem cell factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT 141436-78-4, Protein kinase C
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
IT 60-92-4, CAMP
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of melanoma cell adhesion mol. gene in melanoma by modulation of mRNA synthesis by cAMP, phorbol ester, and **stem cell factor/ c-kit signaling**)
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L78 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:671830** HCAPLUS
DN **130:50592**
ED Entered STN: 23 Oct 1998
TI Lck associates with and is activated by **Kit** in a small cell lung **cancer** cell line: inhibition of **SCF**-mediated growth by the Src family kinase inhibitor PP1
AU Krystal, Geoffrey W.; DeBerry, Candy S.; Linnekin, Diana; Litz, Julie
CS Department of Medicine, Division of Hematology/Oncology, McGuire Veterans Affairs Medical Center, Medical College of Virginia of Virginia Commonwealth University, Richmond, VA, 23249, USA
SO Cancer Research (**1998**), 58(20), 4660-4666
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB At least 70% of small cell lung **cancers** (SCLCs) express the **Kit** receptor tyrosine kinase and its ligand, **stem cell factor** (**SCF**). In an effort to define the **signal** transduction **pathways** activated by **Kit** in SCLC, the authors focused on Src family kinases and, in particular, Lck, a Src-related tyrosine kinase that is expressed in hemopoietic cells and certain **tumors**, including SCLC. **SCF** treatment of the H526 cell line induced a phys. association between **Kit** and Lck that, in vitro, was dependent on phosphorylation of the juxtamembrane domain of **Kit**. Stimulation of **Kit** with recombinant **SCF** resulted in a rapid 3-6-fold increase in the specific activity of Lck, which was similar in magnitude to the activation of Lck resulting from the crosslinking of the T-cell receptor complex of Jurkat cells. Lck activity peaked by 5 min after **SCF** addition, and the elevated activity persisted for at least 30 min in the presence of **SCF**, with kinetics similar to the activation of mitogen-activated protein kinase. PP1, an inhibitor of Src family kinases with selectivity for Lck, completely inhibited **SCF**-mediated growth but had little effect on insulin-like growth **factor**-I-mediated growth. PP1

antagonized both **SCF**-mediated proliferation and inhibition of apoptosis. PP1 had no effect on **Kit** kinase activity but was shown to block total Lck activity by at least 90% by immune complex kinase assay. Low levels of Src, Hck, and Yes were also expressed in the H526 cell line; only Yes showed a consistent increase in specific activity, which was also inhibited by PP1 following **SCF** treatment. These data demonstrate that, in the H526 SCLC cell line, Lck and, possibly, Yes are downstream of **Kit** in a **signal** transduction **pathway**; the inhibition by PP1 of **SCF**-mediated proliferation and inhibition of apoptosis suggests that Src family kinases are intermediates in the **signaling pathways** that regulate these processes.

ST Lck **Kit** kinase **signal** transduction lung **cancer**

IT **Signal transduction, biological**
(Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT c-**Kit** (protein)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT **Stem cell factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT Apoptosis
(Lck kinase role in **stem cell factor** -mediated proliferation and inhibition of apoptosis in human small cell lung **cancer** cell line)

IT Phosphoproteins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp56lck; Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT Phosphorylation, biological
(receptor; Lck association with phosphylated **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT **Lung, neoplasm**
(**small-cell carcinoma**; Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT 141349-91-9, CYes kinase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Lck and Yes activation after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT 114051-78-4 138359-29-2, CKit kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Lck assocs. with and is activated by **Kit** after induction with **stem cell factor** in human small cell lung **cancer** cell line)

IT 67763-96-6, Insulin-like growth factor I
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Lck kinase role in **stem cell factor** -mediated proliferation and inhibition of apoptosis in human small cell lung **cancer** cell line in relation to)

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L78 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1998:651709** HCAPLUS
DN **130:24049**
ED Entered STN: 15 Oct 1998
TI **Stem cell factor** augments FcεRI-mediated TNF-α production and stimulates MAP kinases via a different **pathway** in MC/9 mast cells
AU Ishizuka, Tamotsu; Kawsome, Hideki; Terada, Naohiro; Takeda, Katsuyuki; Gerwins, Par; Keller, Gordon M.; Johnson, Gary L.; Gelfan, Erwin W.
CS Division of Basic Sciences, Dep. of Pediatrics, National Jewish Medical and Research Center, Denver, CO, 80206, USA
SO Journal of Immunology (**1998**), 161(7), 3624-3630
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
CC 15-9 (Immunochemistry)
AB Mast cells express the receptor tyrosine kinase **kit/stem cell factor** receptor (SCFR) which is encoded by the proto-oncogene c-**kit**. Ligation of SCFR induces its dimerization and activation of its intrinsic tyrosine kinase activity leading to

activation of Raf-1, phospholipases, phosphatidylinositol 3-kinase, and extracellular **signal**-regulated kinases. However, little is known about the downstream **signals** initiated by SCFR ligation except for activation of extracellular **signal**-regulated kinases. The murine and mast cell line, MC/9, synthesizes and secretes TNF-α following the aggregation of high affinity Fc receptors for IgE (FcεRI). Ligation of SCFR or FcεRI on MC/9 cells resulted in the activation of all 3 MAP kinase family members, extracellular **signal**-regulated kinases, c-Jun N-terminal kinase (JNK), and p38. **Stem cell factor** (**SCF**)-induced activation of JNK and p38 was insensitive to wortmannin, cyclosporin A, and FK506 whereas activation of these kinases through FcεRI was sensitive to these drugs. Coligation of SCFR augmented FcεRI-mediated activation of MAP kinases, especially JNK activation, and **SCF** augmented FcεRI-mediated TNF-α production in MC/9 cells, although **SCF** alone did not induce TNF-α production This augmentation by **SCF** was regulated at the level of transcription, at least in part, since the promoter activity of TNF-α was enhanced following addition of **SCF**. Thus, **SCF** can augment FcεRI-mediated JNK activation and cytokine gene transcription but via **pathways** that are regulated differently than the ones activated through FcεRI.

ST **stem cell factor** FcepsilonRI TNF MAP kinase mast cell; **tumor** necrosis factor mast cell **stem cell factor** FcepsilonRI

IT Immunoglobulin receptors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IgE type I; **stem cell factor** augments FcεRI-mediated TNF-α production and stimulates MAP kinases via a different **pathway** in MC/9 mast cells)

IT **Tumor** necrosis factors
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**stem cell factor** augments FcεRI-mediated TNF-α formation and stimulates MAP kinases via different **pathway** in MC/9 mast cells)

IT Mast cell
Signal transduction, biological
(**stem cell factor** augments FcεRI-mediated TNF-α production and stimulates MAP kinases via a different **pathway** in MC/9 mast cells)

IT **Stem cell factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**stem cell factor** augments FcεRI-mediated TNF-α production and stimulates MAP kinases via a different **pathway** in MC/9 mast cells)

IT 137632-08-7, Erk2 kinase 137632-08-7 155215-87-5, JNK kinase 165245-96-5, p38 Kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**stem cell factor** augments FcεRI-mediated TNF-α production and stimulates MAP kinases via a different **pathway** in MC/9 mast cells)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L78 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:312127 HCAPLUS
DN 129:93896
ED Entered STN: 28 May 1998
TI Murine **cutaneous mastocytosis** and **epidermal** melanocytosis induced by keratinocyte expression of transgenic **stem cell factor**
AU Kunisada, Takahiro; Lu, Shu-Zhuang; Yoshida, Hisahiro; Nishikawa, Satomi; Nishikawa, Shin-Ichi; Mizoguchi, Masako; Hayashi, Shin-Ichi; Tyrrell, Lynda; Williams, David A.; Wang, Xiaomei; **Longley, B. Jack**
CS Department of Immunology, School of Life Science, Faculty of Medicine, Tottori University, Yonago, 683, Japan
SO Journal of Experimental Medicine (**1998**), 187(10), 1565-1573
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
CC 14-9 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2, 15
AB The growth and differentiation of mast cells and melanocytes require **stem cell factor** (**SCF**), the ligand for the **kit** receptor tyrosine kinase. **SCF** may exist as a membrane-bound or soluble mol. Abnormalities of the **SCF-kit signaling pathway**, with increased local

concns. of soluble **SCF**, have been implicated in the pathogenesis of the human disease **cutaneous mastocytosis**, but have not yet been shown to play a causal role. To investigate both the potential of **SCF** to cause **mastocytosis** and its role in **epidermal** melanocyte homeostasis, we targeted the expression of **SCF** to **epidermal** keratinocytes in mice with two different transgenes controlled by the human keratin 14 promoter. The transgenes contained cDNAs that either produced **SCF**, which can exist in both membrane-bound and soluble forms, or **SCF**, which remains essentially membrane bound. Murine **epidermal** keratinocyte expression of membrane-bound/soluble **SCF** reproduced the phenotype of human **cutaneous mastocytosis**, with **dermal** mast cell infiltrates and **epidermal** **hyperpigmentation**, and caused the maintenance of a population of melanocytes in the interadnexal **epidermis**, an area where melanocytes and melanin are found in human **skin** but where they are not typically found in murine **skin**. Expression of membrane-bound **SCF** alone resulted in **epidermal** melanocytosis and melanin production, but did not by itself cause **mastocytosis**. We conclude, first, that a phenotype matching that of human **mastocytosis** can be produced in mice by keratinocyte overprodn. of soluble **SCF**, suggesting a potential cause of this disease. Second, we conclude that keratinocyte expression of membrane-bound **SCF** results in the postnatal maintenance of **epidermal** melanocytes in mice. Since the resulting animals have **skin** that more closely approximates human **skin** than do normal mice, their study may be more relevant to human melanocyte biol. than the study of **skin** of normal mice.

ST **mastocytosis** melanocyte **stem cell** **factor** keratinocyte

IT **Skin**
(**epidermis**; expression of **stem cell** **factor** by keratinocyte induce murine **cutaneous** **mastocytosis** and **epidermal** melanocytosis)

IT Cell differentiation
Melanocyte
Mouse
(expression of **stem cell factor** by keratinocyte induce murine **cutaneous mastocytosis** and **epidermal** melanocytosis)

IT **Stem cell factor**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(expression of **stem cell factor** by keratinocyte induce murine **cutaneous mastocytosis** and **epidermal** melanocytosis)

IT c-**Kit** (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(expression of **stem cell factor** by keratinocyte induce murine **cutaneous mastocytosis** and **epidermal** melanocytosis)

IT **Skin, disease**
(**hyperpigmentation**; expression of **stem cell** **factor** by keratinocyte induce murine **cutaneous** **mastocytosis** and **epidermal** melanocytosis)

IT **Skin**
(keratinocyte; expression of **stem cell** **factor** by keratinocyte induce murine **cutaneous** **mastocytosis** and **epidermal** melanocytosis)

IT Mast cell
(mastocytoma; expression of **stem cell** **factor** by keratinocyte induce murine **cutaneous** **mastocytosis** and **epidermal** melanocytosis)

IT Cell migration
(of melanocyte; expression of **stem cell factor** by keratinocyte induce murine **cutaneous mastocytosis** and **epidermal** melanocytosis)
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L78 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1992:149933** HCAPLUS
DN **116:149933**
ED Entered STN: 17 Apr 1992
TI The c-**kit** receptor ligand functions as a mast cell chemoattractant
AU Meininger, Cynthia J.; Yano, Hiroshi; Rottapel, Robert; Bernstein, Alan; Zsebo, Krisztina M.; Zetter, Bruce R.
CS Dep. Surg., Harvard Med. Sch., Boston, MA, 02115, USA

SO Blood (**1992**), 79(4), 958-63
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
CC 15-9 (Immunochemistry)
Section cross-reference(s): 2
AB Mast cells accumulate at sites of neovascularization, solid **tumors**, and many immune reactions. Such accumulation requires directed migration of mature mast cells or their precursors. The nature of the chemoattractants that regulate mast cell motility and the identity of the receptors that mediate the chemotactic response are poorly understood. The ability was tested of **stem cell factor** (**SCF**), a mast cell growth factor, to stimulate mast cell migration. The results show that **SCF** is a potent mast cell attractant that stimulates directional motility of both mucosal and connective tissue-type mast cells. The activity is potentiated by costimulation with interleukin-3 (IL-3), another mast cell chemoattractant. **SCF**, a known ligand for the c-**kit** tyrosine kinase receptor, did not stimulate motility in W42 mutant mast cells, which have a defective c-**kit** tyrosine kinase. However, W42 mast cells still migrated in response to IL-3. Thus, **SCF** is a chemotactic factor as well as a growth factor and the c-**kit** receptor can transduce **signals** leading to both cell proliferation and increased directional cell motility.
ST **stem cell factor** mast cell chemotaxis
IT **Signal transduction, biological**
(of chemotactic mobility of mast cells, **stem cell factor** receptors in)
IT Chemotaxis
(of mast cells, **stem cell factor** induction of)
IT Mast cell
(**stem cell factor** as chemoattractant for)
IT Receptors
RL: BIOL (Biological study)
(hematopoietic cell growth factor KL, ligand binding to, mast cell chemotaxis by)
IT **Hemopoietins**
RL: BIOL (Biological study)
(**hematopoietic cell growth factors KL**, receptors, ligand binding to, mast cell chemotaxis by)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 3, **stem cell factor**-induced chemotaxis of mast cell enhancement by)

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L93 ANSWER 1 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-332673 [31] WPIX
CR 2003-201461 [19]; 2003-201462 [19]; 2003-201519 [19]; 2003-201520 [19]; 2003-210306 [20]; 2003-221442 [21]; 2003-221443 [21]; 2003-221534 [21]; 2003-312615 [30]; 2003-371772 [35]; 2003-430378 [40]; 2003-457306 [43]
DNC C2003-086128
TI Use of tyrosine kinase inhibitor for treating allergic diseases e.g. asthma.
DC B03 C02
IN KINET, J; MOUSSY, A
PA (ABSC-N) AB SCI
CYC 101
PI WO 2003002106 A2 20030109 (200331)* EN 42 A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
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EP 1401413 A2 20040331 (200424) EN A61K031-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2003002106 A2 WO 2002-IB3297 20020628; EP 1401413 A2 EP 2002-755512 20020628, WO 2002-IB3297 20020628
FDT EP 1401413 A2 Based on WO 2003002106
PRAI US 2001-301408P 20010629
IC ICM A61K031-00
ICS A61K031-404; A61K031-505; A61K031-506; A61K031-517; A61K031-519
AB WO2003002106 A UPAB: 20040408
NOVELTY - Treatment of allergic diseases involves administration of a tyrosine kinase inhibitor (I) (preferably c-kit inhibitor (Ia)).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating allergic diseases by administration of activated (Ia) obtainable by screening methods (M1) involves:
(i) (a1) contacting activated c-kit (preferably **stem cell factor** activated c-kit wild) and at least one compound to be tested to form a complex;
(ii) (a2) testing and selecting a subset of compounds (c1) inhibiting activated c-kit where the cells are interleukin-3 (IL-3) dependent cells cultured in presence IL-3, to identify a subset of candidate compounds targeting specifically c-kit;
(2) treating allergic diseases by administration of activated (Ia) obtainable by screening method (M2) comprising:
(a) performing a proliferation assay with cells expressing a mutant

c-kit (e.g. in the transphosphorylase domain), with test compounds to identify (c1) targeting activated c-kit by measuring the extent of cell death where the mutant c-kit is a permanent activated c-kit;

(b) performing a proliferation assay with cells expressing c-kit wild, with (c1) identified in (a), where the cells are IL-3 dependent cells cultured in presence of IL-3, to identify a subset of candidate compounds targeting specifically c-kit; and

(c) performing a proliferation assay with cells expressing c-kit, with (c1) identified in (b) and selecting (c1) targeting c-kit wild, by measuring the extent of cell death where (c1) have IC50 less than 10 mu M (preferably less than 1 mu M);

(3) use of (Ia) in the manufacture of a medicament for treating allergic diseases;

(4) a composition (A1) for intranasal or topical administration with an aerosolized formulation to target respiratory tract comprising (I);

(5) an aerosol device preferably with metered dose valve, comprising (A1); and

(6) a nasal dropper or spray device comprising (I) (preferably (Ia).

ACTIVITY - Antiallergic; Antiasthmatic; Antiinflammatory; Immunosuppressive; Dermatological; Antiparasitic. Passive cutaneous anaphylaxis in mice was treated with 4-(4-Methylpiperazine-1-ylmethyl)-N-(4-methyl-3-(4-pyridine-3-yl)pyrimidine-2-ylamino)phenyl)-benzamide (Ib). Mice were administered with (Ib) everyday for 1 week prior antigen challenge at the dosage of 2 mg/day. After a week mice were anesthetized and injected with immunoglubulin E (IgE) (20 ng/20 mu l) and phosphate buffered saline (PBS) in the right and left ears respectively. After 24 hours Evans blue (1%, 100 mu l) containing dinitrophenyl-albumin (100 mu g) were injected in tail vein of mice. Mice were sacrificed after 90 minutes. The ears were cut off and incubated in formamide (1 ml) for 48 hours at 54 deg. C. The results showed that in test animals released prostaglandin 1 and were in good health than the control treated with vehicle.

MECHANISM OF ACTION - Mast cell proliferation inhibitor; Tyrosine kinase inhibitor.

USE - For preventing, delaying and/or treating allergic diseases including asthma, allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic **contact dermatitis**, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis, insect bite skin inflammation and blood sucking parasitic infestation in human, dogs and cats (especially blood sucking parasitic infestation in dogs and cats) (all claimed).

ADVANTAGE - The compounds are potent, non-toxic and selective c-kit wild inhibitor. The treatment is an alternative to the prior art, giving long term effectiveness and tolerance particularly on repeated administration. The selectivity of (I) (preferably (Ia) for its unability to promote death in IL-3 dependent cells cultured in presence of IL-3 gives stability in genetic transfer and hence permits screening efficiently.

Dwg.0/5

FS CPI

FA AB; GI; DCN

MC CPI: B04-F02; B07-D12; B11-C03; B11-C04; B11-C08E; B12-K04; B12-M01A; B14-B02; B14-D06; B14-G02A; B14-K01A; B14-N04; **B14-N17**; **B14-N17C**; C04-F02; C07-D12; C11-C03; C11-C04; C11-C08E; C12-K04; C12-M01A; C14-B02; C14-D06; C14-G02A; C14-K01A; C14-N04; **C14-N17**; **C14-N17C**

TECH UPTX: 20030516

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (A1) is an aqueous and/or an ethanolic solution, a saline solution, colloidal suspension or microcrystalline suspension.

Preferred Device: The aerosol device has a liquid gas system, a suspension aerosol or a pressurized gas system.

Preferred Methods: (M1) further involves testing and selecting (c1) identified in (i). (c1) are inhibitors of mutant activated c-kit and are also capable of inhibiting **stem cell factor** (**SCF**)- activated c-kit wild. The putative inhibitors are tested in (i) and (ii) at a concentration above 10muM and below 1muM respectively. The culture media of IL-3 dependent cells comprises (ng/ml) of IL-3 (0.5 - 10, preferably 1 - 5). The extent of inhibition by (c1) is measured in vivo or in vitro using standard biochemical techniques such as immunoprecipitation and western blot in terms of the amount of c-kit phosphorylation. In (M2) the extent of cell death is measured by 3H-thymidine incorporation, the trypan blue exclusion method or flow cytometry with propidium iodide.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - (I) is selected from the group of N-phenyl-2-pyrimidine-amine derivatives of formula (II).
R1 - R3 = H, F, I, Br, Cl, 1-5C alkyl or (hetero)cyclic group (preferably a pyridyl group);
R4 - R6 = H, F, I, Br, Cl or 1-5C alkyl (preferably methyl); and
R7 = optionally substituted phenyl (preferably 1-benzyl-4-methyl piperazine).
The inhibitor is indolinone, pyrimidine derivative, pyrrolopyrimidine derivative, quinazoline derivative, quinoxaline derivative, pyrazole derivative, bis monocyclic, bicyclic or heterocyclic aryl compound, vinylene-azaindole derivative, pyridyl-quinolones derivative, styryl compound, styryl-substituted pyridyl compound, seleoindole, selenide, tricyclic polyhydroxylic compound or benzylphosphonic acid compound (preferably N-phenyl-2-pyrimidine-amine derivatives, pyrrol-substituted indolinone, monocyclic, bicyclic aryl and heteroaryl compounds or quinazoline derivative).

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The IL-3 dependent cells are mast cells, transfected mast cells, BaF3 or IC-2.

ABEX UPTX: 20030516

SPECIFIC COMPOUNDS - 4-(4-Methylpiperazine-1-ylmethyl)-N-(4-methyl-3-(4-pyridine-3-yl)pyrimidine-2-ylamino)phenyl)-benzamide (Ib) is specifically claimed as (I).

ADMINISTRATION - (I) is administered by topical, oral, intravenous, intramuscular, intra-arterial, intramedullar, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, enteral, sublingual, intranasal or rectal routes (claimed).

L93 ANSWER 2 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-201519 [19] WPIX
CR 2003-201461 [19]; 2003-201462 [19]; 2003-201520 [19]; 2003-210306 [20]; 2003-221442 [21]; 2003-221443 [21]; 2003-221534 [21]; 2003-312615 [30]; 2003-332673 [31]; 2003-371772 [35]; 2003-430378 [40]; 2003-457306 [43]
DNN N2003-160505 DNC C2003-051344
TI Identifying compounds that specifically deplete mast cells, useful for treating disorders such as autoimmune, CNS and inflammatory diseases, allergy, arthritis, bone loss, tumor angiogenesis, and infectious diseases.
DC B04 D16 S03
IN KINET, J; MOUSSY, A
PA (KINE-I) KINET J; (MOUS-I) MOUSSY A; (ABSC-N) AB SCI
CYC 101
PI WO 2003003004 A2 20030109 (200319)* EN 43 G01N033-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
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ZW
US 2003091974 A1 20030515 (200335) C12Q001-00
EP 1434990 A2 20040707 (200444) EN G01N033-50
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FDT EP 1434990 A2 Based on WO 2003003004
PRAI US 2001-22842 20011220; US 2001-301404P 20010629;
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US 2001-301407P 20010629; US 2001-301408P 20010629;
US 2001-301409P 20010629; US 2001-301410P 20010629;
US 2001-301411P 20010629; US 2001-323313P 20010920;
US 2001-323314P 20010920; US 2001-323315P 20010920
IC ICM C12Q001-00; G01N033-00; G01N033-50
ICS G01N033-567
AB WO2003003004 A UPAB: 20040712
NOVELTY - Identifying (M1) compounds capable of depleting mast cells, is new.

DETAILED DESCRIPTION - (M1) comprises:

(a) culturing mast cells in vitro in a suitable culture medium;

(b) adding to the culture medium at least one candidate compound to be tested;

(c) measuring the extent to which the compounds promote mast cells death or interfere with, or inhibit mast cells growth and selecting compounds for which mast cells depletion is observed; and

(d) identifying a subset of compounds that are unable to promote significant death of a cell, is new.

The compounds are non-toxic for other hematopoietic cells that are not mast cells or related cells or cell lines or derived cell lines, such as **SCF** independent expanded human normal CD34+ cells. Step (b) further comprises incubating the cells for prolonged period of time. (M1) alternatively comprises:

(A) providing a culture of mast cells that are wild type mast cells, cell lines derived, activated mutant mast cell lines, or activated wild type mast cells and cell lines derived from it;

(B) contacting the culture of the cells with at least one candidate compound allowing growth and/or survival of mast cells, measuring the level of cell death in the presence of the candidate compound, and comparing the level of cell death in the presence of the candidate compound to the level of cell death in the absence of the compound, where an increase in the level of cell death in the presence of the compound indicates mass cell depletion ability of the candidate compound;

(C) providing a culture of at least one cell other than mast cells that are hematopoietic cells; and

(D) contacting the culture of the cells with at least one compound identified allowing growth and/or survival of the cell, measuring the level of cell death in the presence of the compound, and comparing the level in the absence of the compound, where no significant increase indicates mass cells depletion specificity of the compound versus at least one another hematopoietic cell.

INDEPENDENT CLAIMS are also included for:

(1) a compound obtainable by (M1), where the compound is capable of depleting mast cells and has no significant toxicity for other hematopoietic cells, preferably compounds having an E/S ratio ranging 1/1000 to 1/5;

(2) treating (M2) a disease such as autoimmune diseases, allergy, bone loss, tumor angiogenesis, inflammatory diseases, inflammatory bowel diseases, interstitial cystitis, mastocytosis, infectious diseases and CNS disorders, comprising administering a compound obtainable from (M1); and

(3) promoting (M3) hair growth and hair color revival, comprising administering a compound obtainable from (M1).

ACTIVITY - Neuroprotective; Antipsoriatic; Antiinflammatory; Antiulcer; Antirheumatic; Antiarthritic; Dermatological; Immunosuppressive; Nephrotropic; Hepatotropic; Antiasthmatic; Antiallergic; Cytostatic; Osteopathic; Antibacterial.

No biological data given.

MECHANISM OF ACTION - CD34-Agonist.

USE - The compound is useful to manufacture a medicament for treating disorders such as multiple sclerosis, psoriasis, intestine inflammatory disease, ulcerative colitis, Crohn's disease, rheumatoid arthritis, polyarthritis, local and systemic scleroderma, systemic lupus erythematosus, discoid lupus erythematosus, cutaneous lupus, dermatomyositis, polymyositis, Sjogren's syndrome, nodular panarteritis, autoimmune enteropathy, proliferative glomerulonephritis, vasculitis, active chronic hepatitis and chronic fatigue syndrome, graft-versus-host disease, graft rejection in any organ transplantation including kidney, pancreas, liver, heart, lung and bone marrow, asthma, allergic rhinitis, allergic sinusitis, anaphylactic syndrome, urticaria, angioedema, atopic dermatitis, allergic **contact dermatitis**, erythema nodosum, erythema multiforme, cutaneous necrotizing venulitis, insect bite inflammation, blood sucking parasitic infestation, tumor angiogenesis, mastocytosis, mast cell leukemia, mucositis, interstitial cystitis, osteoporosis, Paget's disease and bacterial infections such as Gram-negative enterobacteria including E. coli, Klebsiella pneumoniae, Serratia marcescens, Citrobactor freudii and Salmonella typhimurium (all claimed).

Dwg.0/0

FS CPI EPI

FA AB; DCN

MC CPI: B04-F04; B11-C08E1; B12-K04E; B14-A01; B14-C03; B14-C09B; B14-E10C; B14-E11; B14-G02C; B14-G02D; B14-H01; B14-K01A; B14-L01; B14-N04; B14-N12; **B14-N17**; **B14-N17C**; B14-S01; D05-H08; D05-H09

EPI: S03-E04D; S03-E14H

TECH UPTX: 20030320

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The mast cells in the method of identifying compounds capable of depleting mast cells are isolated mast cells and cell lines derived from it, BaF3, IC-2 mouse cells, HMC-1, P815 available at American Type Culture Collection (ATCC) under accession no. TIB-64, 10P2 under accession no. CRL-2034, 10P12 under accession no. CRL-2036, 11P0-1 under accession no. CRL-2037 and their derived cell lines. Other hematopoietic cells that are not mast cells or related cells or cell lines are human T lymphocyte Jurkat cell line (ATCC no. TIB-152), human B lymphocyte Daudi or Raji cell line (ATCC no. CCL-213 and CCL-86, respectively), the human monocytic U 937 cell line (ATCC no. CRL-1593.2) and the human HL-60 cell line (ATCC no. CCL-240, cell lines derived with ATCC no. CRL-2258 and CRL-2392) and normal human CD34+ cells that are expanded in a culture medium comprising a cocktail of cytokine except **SCF**. The compounds capable of depleting specifically mast cells at a concentration below 10 muM, preferably below 1 muM, are selected. The compounds exhibiting Ratios E/S from 1/1000 to 1/5, are selected. The cell death assay further comprises a cell proliferation assay, a cell viability assay and/or an apoptosis assay. The extent of cell death is measured by 3H thymidine incorporation, the trypan blue exclusion method, using propidium iodide or by the 51Cr-release assay. The extent of cell death is determined by a test of intracellular esterase activity, and a test of plasma membrane integrity, preferably using fluorescent calcein and ethidium homodimer-1, or by discriminating between

living and dead cells using DiOC18 and propidium iodide, or is measured by fluorometric assays of cell viability and cytotoxicity using a fluorescence microscope, a fluorometer, a fluorescence microplate reader or a flow cytometer. The mast cells that are IL-3 dependent cells are cultured in a culture media comprising IL-3 at a concentration comprised between 0.5-10 ng/ml, preferably 1-5 ng/ml. The compounds are indolinone, pyrimidine derivatives, pyrrolopyrimidine derivatives, quinazolone derivatives, quinoxaline derivatives, pyrazoles derivatives, bis monocyclic, bicyclic or heterocyclic aryl compounds, vinylene-azaindole derivatives and pyridyl-quinolones derivatives, styryl compounds, styryl-substituted pyridyl compounds, seleoindoles, selenides, tricyclic polyhydroxylic compounds or benzylphosphonic acid compounds. (M3) further comprises administering at least one antibiotic, preferably dapsone, azathioprine, erythromycin, propionyleryhtromycin, neomycin, gentamycin, tobramycin and mechlocycline, bacitracin, cephalosporins, aminoglycosides, tetracyclines, streptomycins.

ABEX UPTX: 20030320

ADMINISTRATION - The route of administration of the compound is via aerolized formulations to target areas of a patient's respiratory tract, or via the intranasal or topical routes (claimed).
No dosage given.

EXAMPLE - No suitable example given.

L93 ANSWER 3 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-687622 [67] WPIX
DNC C2000-209364
TI Prevention and treatment of **contact dermatitis**, hyperpigmentation, cutaneous inflammation and other conditions, comprises inhibiting the **stem cell factor signaling** pathway.
DC B04 D16 D21
IN **LONGLEY, B J**
PA (UYCO) UNIV COLUMBIA NEW YORK; (LONG-I) LONGLEY B J
CYC 90
PI WO 2000067794 A1 20001116 (200067)* EN 72 A61K039-395
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
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AU 2000048253 A 20001121 (200112) A61K039-395
US 2002123031 A1 20020905 (200260) C12Q001-00
US 6576812 B1 20030610 (200340) G01N033-00
ADT WO 2000067794 A1 WO 2000-US12405 20000505; AU 2000048253 A AU 2000-48253 20000505; US 2002123031 A1 CIP of US 1999-306143 19990506, US 1999-474478 19991229; US 6576812 B1 US 1999-306143 19990506
FDT AU 2000048253 A Based on WO 2000067794
PRAI US 1999-474478 19991229; US 1999-306143 19990506
IC ICM A61K039-395; C12Q001-00; G01N033-00
ICS A01K067-00; A01K067-027; A01K067-033; C07K016-00; C12Q001-70
AB WO 200067794 A UPAB: 20001223
NOVELTY - Preventing or treating diseases comprises administering a compound capable of inhibiting the **stem cell factor signaling** pathway.
DETAILED DESCRIPTION - Preventing or treating **contact dermatitis**, hyperpigmentation, asthma, cutaneous inflammation, anaphylaxis or bronchospasm, mastocytosis, urticaria, hypersensitivity, airway inflammation, interstitial cystitis or a tumor which expresses activated kit comprises administering to the subject a compound capable of inhibiting the **stem cell factor signaling** pathway effective to prevent or treat the conditions.

INDEPENDENT CLAIMS are also included for the following:
(1) providing contraception comprising administering a compound capable of inhibiting the cell factor **signaling** pathway effective to prevent conception;
(2) desensitizing a subject to an agent comprising administering to the subject, during the afferent phase of an immune response, a compound capable of inhibiting the **stem cell factor** **signaling** pathway effective to desensitize the subject;
(3) identifying a composition, compound or procedure which can produce a skin response comprising administering the compound or composition or applying the procedure to transgenic mice which express endogenous epidermal **stem cell factor** and analyzing the skin of the transgenic mice for a response;
(4) identifying a composition, compound or procedure which can reduce skin response in a subject comprises administering the composition or compound or applying the procedure to the transgenic mice which express endogenous epidermal **stem cell factor** and which had been induced to produce a skin disease and analyzing the skin to determine the reduction of the skin response;
(5) identifying a compound, composition or procedure which can reduce radiation damage to skin comprises administering the composition or compound or applying the procedure to the skin of the transgenic mice which express endogenous epidermal **stem cell factor**, subjecting the skin of the transgenic mice and control mice to radiation and analyzing the effects of the composition, compound or procedure on reducing skin radiation damage;
(6) a composition for treating human skin diseases comprising a compound that can treat skin diseases of the transgenic mice which express endogenous epidermal **stem cell factor** and a carrier, wherein the compound specifically targets the epidermal **stem cell factor** or its receptor.
ACTIVITY - Dermatological; antiinflammatory; antiasthmatic; antiinflammatory; antiallergic; immunosuppressive; cytostatic. No biological data is given.
MECHANISM OF ACTION - **Stem cell factor** **signaling** pathway inhibitor.
USE - The methods can be used to treat and/or prevent **contact dermatitis**, hyperpigmentation, asthma, cutaneous inflammation, anaphylaxis or bronchospasm , mastocytosis, urticaria, hypersensitivity, airway inflammation e.g. rhinitis, interstitial cystitis, a tumor which expresses activated kit wherein the tumor is e.g. a gastrointestinal stromal tumor or a germ cell tumor or radiation damage. The method may also be used to provide contraception (claimed).
Dwg.0/13

FS CPI
FA AB; DCN
MC CPI: B04-E01; B04-G01; B04-G21; **B04-H16**; **B04-M01**; B04-N04; B11-C08E2; B12-K04E; B14-C03; B14-H01; B14-K01; B14-K01A; B14-N07B; **B14-N17**; **B14-N17C**; B14-P01; B14-S06; D05-H09; D05-H11A; D05-H12; D05-H16A
TECH UPTX: 20001223
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Methods: The methods comprise inhibiting the kinase enzymatic reaction of kit protein, inhibiting chymase, elastase or other **SCF** cleaving enzymes, inhibiting ligand binding with an antibody, peptide or nonpeptide chemical, inhibiting kit dimerization with an antibody, peptide or nonpeptide chemical, inhibiting downstream **signaling** of the kit activation pathway by blocking substrate association with the kit kinase domain, inhibiting downstream **signaling** of the kit activation pathway by blocking enzymatic function in the downstream **signaling** pathway or inhibiting the kit activation pathway by blocking binding of molecules in the downstream **signaling** pathway. The compound is preferably an antibody or portion thereof, preferably a monoclonal

antibody which is a human, humanized or chimeric antibody. The monoclonal antibody is preferably an anti-kit antibody , especially ACK2. The compound may comprise a Fab fragment of an anti-kit antibody or the variable domain of an anti-kit antibody. The compound may comprise one or more CDR portions of an anti-kit antibody. The antibody is preferably selected form immunoglobulin (Ig)A, IgD, IgE, IgG and IgM. The compound may also be a peptide, peptidomimetic, a nucleic acid or an organic compound with a molecular weight less than 500 Daltons. The compounds may be sSCF, SKIT ligand or a fragment of them. In the method for identifying a compound, composition or procedure which can reduce radiation damage, the radiation damage may be due to ultraviolet light, tanning, carcinogenesis, photo-aging, photo damage or development of melanoma. The epidermal **stem cell factor** transgene encodes either a membrane bound epidermal **stem cell factor** or a membrane/soluble epidermal **stem cell factor.** In the method for reducing skin response the skin response can be induced by applying an irritant or an allergic dermatitis inducing agent to the skin e.g. croton oil or dinitrofluorobenzene. In the method for testing for skin response compounds which may be tested include cosmetics, medications and skin care products.

ABEX UPTX: 20001223

ADMINISTRATION - Administration is intralesional, intraperitoneal, intramuscular, subcutaneous, intravenous, by liposome mediate delivery, transmucosal, intestinal, topical, nasal, oral, anal, ocular, otic, intravesicular or parenteral. No dosage is specified.

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COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED: 9 AUG 2004      <20040809/UP>
PATENTS CITATION INDEX, COVERS 1973 TO DATE

>>>  LEARNING FILE LDPCI AVAILABLE  <<<

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L94  ANSWER 1 OF 2  DPCI  COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2001-483040 [52]   DPCI
DNC  C2001-144762
TI   Treatment of mastocytosis involves administering indolinone derivatives or
     its salt to the patient.
DC   B02
IN   LONGLEY, B J
PA   (UYCO) UNIV COLUMBIA NEW YORK
CYC  94
PI   WO 2001047517 A1 20010705 (200152)* EN   44p    A61K031-40
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     AU 2001026083 A  20010709 (200164)              A61K031-40
     US 6339100    B1 20020115 (200208)              A61K031-40
ADT  WO 2001047517 A1 WO 2000-US35597 20001229; AU 2001026083 A AU 2001-26083
     20001229; US 6339100 B1 US 1999-474474 19991229
FDT  AU 2001026083 A Based on WO 2001047517
PRAI US 1999-474474       19991229
IC   ICM  A61K031-40
     ICS  A61K031-495
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FS CPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 20020731

NCL US 6339100 B1 20020115
000/514.255; 000/514.412

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	4	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	2	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	1	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	35	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20030709

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
US 6339100	B1	US 5883116	A 1999-214132/18
	PA:	(SUGE-N) SUGEN INC	
	IN:	**MCMAHON, G; SUN, L; TANG, P C**	
		US 5905149	A 1998-042101/04
	PA:	(PHAA) PHARMACIA & UPJOHN SPA	
	IN:	**BALLINARI, D; BATTISTINI, C; BUZZETTI, F; ERMOLI, A; VIOGLIO, S**	
		WO 9910325	A1 1999-190570/16
	PA:	(GLAX) GLAXO GROUP LTD; (GLAX) GLAXO WELLCOME INC	
	IN:	**DICKERSON, S; HARRIS, P A; HUNTER, R N; JUNG, D K; LACKEY, K E; MCNUTT, R W; PEEL, M R; VEAL, J M; DICKERSON, S H**	
		WO 9961422	A1 2000-086692/07
	PA:	(SUGE-N) SUGEN INC	
	IN:	**MCMAHON, G; SUN, L; TANG, P C**	
WO 200147517	A A	US 5883116	A 1999-214132/18
	PA:	(SUGE-N) SUGEN INC	
	IN:	**MCMAHON, G; SUN, L; TANG, P C**	
	A	US 5905149	A 1998-042101/04
	PA:	(PHAA) PHARMACIA & UPJOHN SPA	
	IN:	**BALLINARI, D; BATTISTINI, C; BUZZETTI, F; ERMOLI, A; VIOGLIO, S**	
	A	WO 9910325	A1 1999-190570/16
	PA:	(GLAX) GLAXO GROUP LTD; (GLAX) GLAXO WELLCOME INC	
	IN:	**DICKERSON, S; HARRIS, P A; HUNTER, R N; JUNG, D K; LACKEY, K E; MCNUTT, R W; PEEL, M R; VEAL, J M; DICKERSON, S H**	
	A	WO 9961422	A1 2000-086692/07
	PA:	(SUGE-N) SUGEN INC	
	IN:	**MCMAHON, G; SUN, L; TANG, P C**	

REN LITERATURE CITATIONS UPR: 20020731

Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
US 6339100	B1	Anderson, D.M., et al. (1990) "Molecular cloning of mast cell growth factor, a hematopoietin that is active in both membrane bound and soluble forms" Cell, 63:235-243 (Exhibit 1).
US 6339100	B1	Bradl, M., et al. (1991) "Clonal coat color variation due to a transforming gene expressed in melanocytes of transgenic mice" Proc. Nat. Acad. Sci. USA 88:6447-6451; (Exhibit 2).
US 6339100	B1	Costa, J. J. et al. (1996) "Recombinant human stem cell factor (KIT ligand) promotes human mast cell and melanocyte hyperplasia and functional activation in vivo" J. Exp. Med 183: 2681-2686; (Exhibit 3).
US 6339100	B1	Funasaka, Y., et al. (1992) "C-kit-kinasse induces a cascade of protein tyrosine phosphorylation in normal human melanocytes in respnse to mast cell growth factor and stimulates mitogen-activated protein kinase but is down-regulated in melanomas" Mol. Biol. Cell, 3:197-209; (Exhibit 4).
US 6339100	B1	Furitsu, T., et al. (1993) Identification of mutations in the coding sequence of the proto-oncogene c-kit in human mast cell leuemia cell line causing ligand independent activation of c-KIT product J. Clin. Invest., 92:1736-1744; (Exhibit 5).
US 6339100	B1	Grichnik, J. M., et al. (1995) "Human recombinant stem-cell factor induces melanocytic hyperplasia in susceptible patients" J. Am. Acad. Dermol., 33: 577-583; (Exhibit 6).
US 6339100	B1	Hamann, K., et al. (1995) "Expression of stem cell factor in cutaneous mastocytosis" Br. J. Dermatol., 133: 203-208; (Exhibit 7).
US 6339100	B1	Harrist, T.J., et al. (1995) Recombinant human stem cell factor in (SCF) (c-kit ligand promotes melanocytes hyperplasia and activation in vivo Lab. Invest., 72:48A; (Exhibit 8).
US 6339100	B1	Hirobe, T. (1984) "Histochemical survey of the distribution of the epidermal melanoblasts and melanocytes in the mouse during fetal and postnatal periods" Anat. Rec., 208:589-594; (Exhibit 9).
US 6339100	B1	Longley, B. J. et al. (1993) "Altered metabolism of mast-cell growth factor (c-kit ligand) in cutaneous mastocytosis" N. Engl. J. Med. . 328:1302-1307; (Exhibit 10).
US 6339100	B1	Longley, B. J. et al. (1995) "The mast cell and mast cell disease" J. Am. Acad. Dermatol., 32:545-561; (Exhibit 11).
US 6339100	B1	Longley, B. J., et al. (1996) "Somastic c-KIT activating mutation in urticaria pigmentosa and aggressive mastocytosis: establishment of clonality in a human mast cell neoplasm" Nature Genetics, 12:312-314; (Exhibit 12).
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cell-conditioned medium" J. Biol. Chem., 266:8102-8107; (Exhibit 13).

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US 6339100 B1 Martin FH, Suggs SV, Langley KE, Lu HS, Ting J, et al: Primary structure and functional expression of rat and human stem cell factor DNAs. Cell 63: 203-211, 1990 (Exhibit 27).

US 6339100 B1 Mohammadi M, McMahon G, Sun L, Tang C, Hirth P, et al: Structures of the tyrosine kinase domain of fibroblast growth factor receptor in complex with

inhibitors. Science 276: 955-960, 1997 (Exhibit 28).

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US 6339100 B1 Galli, Stephen J. and Mekori, Yoseph A., "Undiminished Immunologic Tolerance to Contact Sensitivity in Mast Cell-Deficient W/Wv and S1/S1d Mice1", The Journal of Immunology. (1995), vol. 135, No. 2, pp. 879-885 (Exhibit 34).

US 6339100 B1 Askenase, Philip W., Loveren, Henk Van, Kraeuter-Kops, Sandra, Ron, Yacov, Meade, Robin, Theoharides, Theoharis C., Nordlund, James J., Scovern, Henry, Gerhson, Michael D., and Ptak, Wlodzimierz., "Defective Elicitation of Delayed-Type Hypersensitivity in W/Wv and SI/SId Mast Cell-Deficient Mice1", The Journal of Immunology. (1983), vol. 131, No. 6, pp. 2687-2693 (Exhibit 35).

CGP CITING PATENTS UPG: 20040108

Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
WO 200147517	A1 XP	WO 2003002105 A	2003-201461/12
	PA:	(ABSC-N) AB SCI	
	IN:	**KINET, J; MOUSSY, A**	
	XP	WO 2003002114 A	2003-312615/32
	PA:	(ABSC-N) AB SCI	
	IN:	**KINET, J; MOUSSY, A**	

L94 ANSWER 2 OF 2 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-687622 [67] DPCI
DNC C2000-209364

TI Prevention and treatment of contact dermatitis, hyperpigmentation, cutaneous inflammation and other conditions, comprises inhibiting the stem cell factor signaling pathway.
DC B04 D16 D21
IN **LONGLEY, B J**
PA (UYCO) UNIV COLUMBIA NEW YORK; (LONG-I) LONGLEY B J
CYC 90
PI WO 2000067794 A1 20001116 (200067)* EN 72p A61K039-395
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000048253 A 20001121 (200112) A61K039-395
US 2002123031 A1 20020905 (200260) C12Q001-00
US 6576812 B1 20030610 (200340) G01N033-00
ADT WO 2000067794 A1 WO 2000-US12405 20000505; AU 2000048253 A AU 2000-48253 20000505; US 2002123031 A1 CIP of US 1999-306143 19990506, US 1999-474478 19991229; US 6576812 B1 US 1999-306143 19990506
FDT AU 2000048253 A Based on WO 2000067794
PRAI US 1999-474478 19991229; US 1999-306143 19990506
IC ICM A61K039-395; C12Q001-00; G01N033-00
ICS A01K067-00; A01K067-027; A01K067-033; C07K016-00; C12Q001-70
FS CPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 20030929

NCL US 6576812 B1 20030610
000/800.130; 000/800.140; 000/800.180; 000/800.300

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	3	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	1	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	1	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	1	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	27	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20030929

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
US 6576812	B1	US 5877396	A 1995-382849/49
		PA: (SLOK) SLOAN KETTERING INST CANCER RES	
		IN: **CLYNES, R; ONO, M; RAVETCH, J V; SYLVESTRE, D; TAKAI, T**	
		US 5911988	A 1999-357170/30
		PA: (FARB) BAYER CORP; (UNMI) UNIV MICHIGAN	
		IN: **BROWNELL, E; KUNKEL, S L; LUKACS, N; STRIETER, R M**	

US 5997865 A 1995-358636/46
PA: (GETH) GENENTECH INC; (BENN-I) BENNETT B D; (BROZ-I) BROZ S D; (MATT-I) MATTHEWS W; (ZEIG-I) ZEIGLER F C
IN: **BENNETT, B D; BROZ, S D; MATTHEWS, W; ZEIGLER, F C**

WO 200067794 A A US 5877396 A 1995-382849/49
PA: (SLOK) SLOAN KETTERING INST CANCER RES;
IN: **CLYNES, R; ONO, M; RAVETCH, J V; SYLVESTRE, D; TAKAI, T**
US 5911988 A 1999-357170/30
PA: (FARB) BAYER CORP; (UNMI) UNIV MICHIGAN
IN: **BROWNELL, E; KUNKEL, S L; LUKACS, N; STRIETER, R M**
US 5997865 A 1995-358636/46
PA: (GETH) GENENTECH INC; (BENN-I) BENNETT B D; (BROZ-I) BROZ S D; (MATT-I) MATTHEWS W; (ZEIG-I) ZEIGLER F C
IN: **BENNETT, B D; BROZ, S D; MATTHEWS, W; ZEIGLER, F C**

REN LITERATURE CITATIONS UPR: 20030929

Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
US 6576812	B1	CA Kappel et al., Current Opinion in Biotechnology, "Regulating gene expression in transgenic animals," 1992, 3:548-553.*
US 6576812	B1	L-M Houdebine, Journal of Biotechnology, "Production of pharmaceutical proteins from transgenic animals," 1994, 34:269-287.*
US 6576812	B1	CD Sigmund, Arterioscler Thromb Vasc Biol., "Viewpoint: Are Studies in Genetically Altered Mice Out of Control?" 2000, 20:1425-1429.*
US 6576812	B1	RJ Wall, Theriogenology, "Transgenic Livestock: Progress and Prospects for the Future," 1996, 45:57-68.*
US 6576812	B1	Anderson, D.M., et al. (1990) "Molecular cloning of mast cell growth factor, a hematopoietin that is active in both membrane bound and soluble forms" Cell, 63:235-243 (Exhibit 2).
US 6576812	B1	Bradl, M., et al. (1991) "Clonal coat color variation due to a transforming gene expressed in melanocytes of transgenic mice" Proc. Nat. Acad. Sci. USA 88:6447-6451 (Exhibit 3).
US 6576812	B1	Costa, J. J. et al. (1996) "Recombinant human stem cell factor (KIT ligand) promotes human mast cell and melanocyte hyperplasia and functional activation in vivo" J. Exp. Med 183:2681-2686 (Exhibit 4).
US 6576812	B1	Funasaka, Y., et al. (1992) "C-kit-kinasse induces a cascade of protein tyrosine phosphorylation in normal human melanocytes in respnse to mast cell growth factor and stimulates mitogen-activated protein kinase but is down-regulated in melanomas" Mol. Biol. Cell, 3:197-209 (Exhibit 5).
US 6576812	B1	Furitsu, T., et al. (1993) "Identification of mutations in the coding sequence of the proto-oncogene c-kit in human mast cell leuemia cell line causing ligand independent activation of c-KIT product" J. Clin. Invest., 92:1736-1744

(Exhibit 6).

US 6576812 B1 Grichnik, J. M., et al. (1995) "Human recombinant stem-cell factor induces melanocytic hyperplasia in susceptible patients" J. Am. Acad. Dermol., 33: 577-583 (Exhibit 7).

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US 6576812 B1 Harrist, T.J., et al. (1995) Recombinant human stem cell factor in (SCF) (c-kit ligand promotes melanocytes hyperplasia and activation in vivo Lab. Invest., 72:48A (Exhibit 9).

US 6576812 B1 Hirobe, T. (1984) "Histochemical survey of the distribution of the epidermal melanoblasts and melanocytes in the mouse during fetal and postnatal periods" Anat. Rec., 208:589-594 (Exhibit 10).

US 6576812 B1 Longley, B. J. et al. (1993) "Altered metabolism of mast-cell growth factor (c-kit ligand) in cutaneous mastocytosis" N. Engl. J. Med. . 328:1302-1307 (Exhibit 11).

US 6576812 B1 Longley, B. J. et al. (1995) "The mast cell and mast cell disease" J. Am. Acad. Dermatol., 32:545-561 (Exhibit 12).

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US 6576812 B1 Lu, H. S., et al. (1991) "Amino acid sequence and post-translational modification of stem cell factor isolated from buffalo rat liver cell-conditioned medium" J. Biol. Chem., 266:8102-8107 (Exhibit 14).

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US 6576812 B1 Okura, M., et al. (1995) "Effects of monoclonal anti-c-kit antibody (AKC2) on melanocytes in newborn mice" J. Invest. Dermatol., 105:322-328 (Exhibit 16).

US 6576812 B1 Tsai, M., et al. (1991) "The rat c-kit ligand, stem cell factor, induces the development of connective tissue-type and mucosal mast cells in vivo: analysis by anatomical distribution, hisochemistry, and protease phenotype" J. Exp. Med., 174:125-131 (Exhibit 17).

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US 6576812 B1 Weiss, R. R. et al. (1995) "Human dermal endothelial cells express membrane-associated mast cell growth factor" J. Invest. Dermatol. 104:101-106 (Exhibit 19).

US 6576812 B1 Williams, D.E., et al. (1990) "Identification of a ligand for the c-kit proto-oncogene" Cell, 1990;63:167-174 (Exhibit 20).

US 6576812 B1 Yarden, Y., et al. (1987) "Human proto-oncogene c-kit: a new cell surface receptor tyrosine kinase for an unidentified ligand" EMBO J. 6:3341-3351

(Exhibit 21).

US 6576812 B1 Yoshida, H., et al. (1996) "Distinct stages of melanocyte differentiation revealed by analysis of nonuniform pigmentation patterns" Development, 122:1207-1214 (Exhibit 22).

US 6576812 B1 Yohida, H. et al. (1996) "Neural and skin cell-specific expression pattern conferred by Steel factor regulatory sequence in transgenic mice" Development Dynamic, 207:222-232 (Exhibit 23).

US 6576812 B1 Zsebo, K. M., et al. (1990) "Stem cell factor is encoded at the S1 locus of the mouse and is the ligand for the c-kit tyrosine kinase receptor" Cell, 63:213-224 (Exhibit 24).

CGP CITING PATENTS UPG: 20040505

Cited by Examiner

CITED PATENT	CAT	CITING PATENT	ACCNO
WO 200067794	A X	WO 2003024386 A	2003-371772/32
	PA:	(ABSC-N) AB SCI	
	IN:	**KINET, J; MOUSSY, A**	

=> => fil medline
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FILE LAST UPDATED: 12 AUG 2004 (20040812/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L114 ANSWER 1 OF 2 MEDLINE on STN
AN 1999002668 MEDLINE
DN PubMed ID: 9788619
TI Lck associates with and is activated by Kit in a small cell lung cancer cell line: **inhibition** of SCF-mediated growth by the Src family kinase **inhibitor** PP1.
AU Krystal G W; DeBerry C S; Linnekin D; Litz J
CS Department of Medicine, Medical College of Virginia Commonwealth University, McGuire Veterans Affairs Medical Center, Richmond 23249, USA.. GKRYSTAL@GEMS.VCU.edu
SO Cancer research, **(1998 Oct 15)** 58 (20) 4660-6.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811

ED Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981106

AB At least 70% of small cell lung cancers (SCLCs) express the Kit receptor tyrosine kinase and its ligand, stem cell factor (SCF). In an effort to define the **signal** transduction **pathways** activated by Kit in SCLC, we focused on Src family kinases and, in particular, Lck, a Src-related tyrosine kinase that is expressed in hemopoietic cells and certain tumors, including SCLC. SCF treatment of the H526 cell line induced a physical association between Kit and Lck that, in vitro, was dependent on phosphorylation of the juxtamembrane domain of Kit. Stimulation of Kit with recombinant SCF resulted in a rapid 3-6-fold increase in the specific activity of Lck, which was similar in magnitude to the activation of Lck resulting from the cross-linking of the T-cell receptor complex of Jurkat cells. Lck activity peaked by 5 min after SCF addition, and the elevated activity persisted for at least 30 min in the presence of SCF, with kinetics similar to the activation of mitogen-activated protein kinase. PP1, an **inhibitor** of Src family kinases with selectivity for Lck, completely **inhibited** SCF-mediated growth but had little effect on insulin-like growth factor-I-mediated growth. PP1 antagonized both SCF-mediated proliferation and **inhibition** of apoptosis. PP1 had no effect on Kit kinase activity but was shown to block total Lck activity by at least 90% by immune complex kinase assay. Low levels of Src, Hck, and Yes were also expressed in the H526 cell line; only Yes showed a consistent increase in specific activity, which was also **inhibited** by PP1 following SCF treatment. These data demonstrate that, in the H526 SCLC cell line, Lck and, possibly, Yes are downstream of Kit in a **signal** transduction **pathway**; the **inhibition** by PP1 of SCF-mediated proliferation and **inhibition** of apoptosis suggests that Src family kinases are intermediates in the **signaling pathways** that regulate these processes.

CT Check Tags: Human; Support, U.S. Gov't, Non-P.H.S.
***Carcinoma, Small Cell: DT, drug therapy**
Carcinoma, Small Cell: ME, metabolism
***Enzyme Inhibitors: PD, pharmacology**
Jurkat Cells
***Lung Neoplasms: DT, drug therapy**
Lung Neoplasms: ME, metabolism
*Lymphocyte Specific Protein Tyrosine Kinase p56(lck): PH, physiology
*Proto-Oncogene Protein c-kit: PH, physiology
Pyrazoles: PD, pharmacology
Pyrimidines: PD, pharmacology
Signal Transduction
***Stem Cell Factor: AI, antagonists & inhibitors**
Stem Cell Factor: PD, pharmacology
***src-Family Kinases: AI, antagonists & inhibitors**

CN 0 (4-amino-5-(4-methylphenyl)-7-(tert-butyl)pyrazolo(3,4-d)pyrimidine); 0 (Enzyme **Inhibitors**); 0 (Pyrazoles); 0 (Pyrimidines); 0 (Stem Cell Factor); EC 2.7.1.112 (Proto-Oncogene Protein c-kit); EC 2.7.1.112 (src-Family Kinases); EC 2.7.1.37 (Lymphocyte Specific Protein Tyrosine Kinase p56(lck))

L114 ANSWER 2 OF 2 MEDLINE on STN
AN 97304300 MEDLINE
DN PubMed ID: 9160663
TI Macrophage inflammatory protein-1alpha and interferon-inducible protein 10 **inhibit** synergistically induced growth factor stimulation of MAP kinase activity and suppress phosphorylation of eukaryotic initiation factor 4E and 4E binding protein 1.
AU Aronica S M; Gingras A C; Sonenberg N; Cooper S; Hague N; Broxmeyer H E
CS Department of Microbiology/Immunology, Walther Oncology Center, Indiana University School of Medicine, Indianapolis 46202-5121, USA.

SO Blood, **(1997 May 15)** 89 (10) 3582-95.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199706
ED Entered STN: 19970630
Last Updated on STN: 19980206
Entered Medline: 19970619

AB Granulocyte-macrophage colony-stimulating factor (GM-CSF) and Steel factor (SLF) synergistically stimulate Raf-1 kinase activity, protein synthesis, and proliferation in hematopoietic MO7e cells; synergistic action of these factors is blocked by the suppressive chemokines macrophage inflammatory protein-1alpha (MIP-1alpha) and interferon-inducible protein 10 (IP-10; Aronica et al, J Biol Chem 270:21998, 1995). We assessed the potential for both stimulatory and **inhibitory** factors to act through the MAP kinase **signaling pathway** by studying the effects of growth factors and chemokines on MAP kinase activation. Also, because activation of kinase **signaling pathways** and stimulation of protein synthesis by peptide growth factors are associated with increased phosphorylation of eukaryotic initiation factor 4E (eIF-4E) and the translational repressor 4E-binding protein 1 (4E-BP1) in some target cells, we investigated whether growth factor treatment could alter eIF-4E or 4E-BP1 phosphorylation state in MO7e cells. We report that treatment of MO7e cells with GM-CSF and SLF stimulated significant, greater-than-additive increases in MAP kinase activity and the phosphorylation of both eIF-4E and 4E-BP1. Increased 4E-BP1 phosphorylation correlated with a decrease in the association of 4E-BP1 with eIF-4E. Growth factor-induced phosphorylation of 4E-BP1 and dissociation of 4E-BP1 from eIF-4E was blocked in cells treated with rapamycin, wortmannin, or PD098059. Treatment of cells with IP-10 or MIP-1alpha blocked the stimulatory effects of GM-CSF and SLF, resulting in suppression of MAP kinase activity, eIF-4E and 4E-BP1 phosphorylation, and eIF-4E/4E-BP1 dissociation. Our results suggest that GM-CSF and SLF exert part of their combined growth-promoting effects on MO7e cells through activation of MAP kinase and enhancement of eIF-4E and 4E-BP1 phosphorylation and dissociation and that suppression of growth factor-induced protein synthesis by MIP-1alpha and IP-10 involves translational repression at the level of eIF-4E.

CT Check Tags: Human
8-Bromo Cyclic Adenosine Monophosphate: PD, pharmacology
*Ca(2+)-Calmodulin Dependent Protein Kinase: ME, metabolism
*Carrier Proteins
*Chemokines, CXC
Cyclic AMP: PD, pharmacology
*Cytokines: PD, pharmacology
Drug Synergism
Enzyme Activation: DE, drug effects
Eukaryotic Initiation Factor-4E
Forskolin: PD, pharmacology
***Granulocyte-Macrophage Colony-Stimulating Factor: AI, antagonists & inhibitors**
Granulocyte-Macrophage Colony-Stimulating Factor: PD, pharmacology
***Growth Inhibitors: PD, pharmacology**
Leukemia, Megakaryocytic, Acute: PA, pathology
*Macrophage Inflammatory Protein-1: PD, pharmacology
Neoplasm Proteins: ME, metabolism
*Peptide Initiation Factors: ME, metabolism
*Phosphoproteins: ME, metabolism
Phosphorylation: DE, drug effects
*Protein Processing, Post-Translational: DE, drug effects
Recombinant Proteins: AI, antagonists & inhibitors

Recombinant Proteins: PD, pharmacology
Signal Transduction: DE, drug effects
***Stem Cell Factor: AI, antagonists & inhibitors**
Stem Cell Factor: PD, pharmacology
Tumor Cells, Cultured: DE, drug effects
RN 23583-48-4 (8-Bromo Cyclic Adenosine Monophosphate); 60-92-4 (Cyclic AMP); 66428-89-5 (Forskolin); 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor)
CN 0 (CXC chemokine IP-10); 0 (Carrier Proteins); 0 (Chemokines, CXC); 0 (Cytokines); 0 (Eukaryotic Initiation Factor-4E); 0 (Growth **Inhibitors**); 0 (Macrophage Inflammatory Protein-1); 0 (Neoplasm Proteins); 0 (PHAS-I protein); 0 (Peptide Initiation Factors); 0 (Phosphoproteins); 0 (Recombinant Proteins); 0 (Stem Cell Factor); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase)

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COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

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RECORDS LAST ADDED: 11 August 2004 (20040811/ED)

FILE RELOADED: 19 October 2003.

=> d l119 all tot

L119 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:357104 BIOSIS
DN PREV199900357104
TI **SCF**-KIT pathway in human epidermal melanocyte homeostasis (and reply).
AU **Longley, B. Jack** [Reprint author]; Carter, Eric L.; Grichnik, James M.
CS Section of Dermopathology, College of Physicians and Surgeons, Columbia University, 630 West 168 Street, VC 5-578, New York, NY, 10032, USA
SO Journal of Investigative Dermatology, (July, 1999) Vol. 113, No. 1, pp. 139-140. print.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Letter
LA English
ED Entered STN: 2 Sep 1999
Last Updated on STN: 2 Sep 1999
CC Integumentary system - General and methods 18501
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Metabolism - General metabolism and metabolic pathways 13002
Endocrine - General 17002
IT Major Concepts
Chemical Coordination and Homeostasis; Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
epidermis: integumentary system; melanocytes: integumentary system, homeostasis
IT Chemicals & Biochemicals
stem cell factor; KIT: activation
ORGN Classifier
Hominidae 86215
Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L119 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:263271 BIOSIS
DN PREV199900263271
TI Inhibition of spontaneous receptor phosphorylation by residues in a putative alpha-helix in the KIT intracellular juxtamembrane region.
AU Ma, Yongsheng; Cunningham, Matthew E.; Wang, Xiaomei; Ghosh, Indraneel; Regan, Lynn; **Longley, B. Jack** [Reprint author]
CS Dept. of Dermatology, Section of Dermatopathology, College of Physicians and Surgeons, Columbia University, 630 West 168th St., Vanderbilt Clinic 15-221, New York, NY, 10032, USA
SO Journal of Biological Chemistry, (May 7, 1999) Vol. 274, No. 19, pp. 13399-13402. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999
AB KIT receptor kinase activity is repressed, prior to **stem cell factor** binding, by unknown structural constraints. Using site-directed mutagenesis, we examined the role of KIT intracellular juxtamembrane residues Met-552 through Ile-563 in controlling receptor auto-phosphorylation. Alanine substitution for Tyr-553, Trp-557, Val-559, or Val-560, all sitting along the hydrophobic side of an amphipathic alpha-helix (Tyr-553-Ile-563) predicted by the Chou-Fasman algorithm, resulted in substantially increased spontaneous receptor phosphorylation, revealing inhibitory roles for these residues. Alanine substitution for other residues, most of which are on the hydrophilic side of the helix, caused no or slightly increased basal receptor phosphorylation. Converting Tyr-553 or Trp-557 to phenylalanine generated slight or no elevation, respectively, in basal KIT phosphorylation, indicating that the phenyl ring of Tyr-553 and the hydrophobicity of Trp-557 are critical for the inhibition. Although alanine substitution for Lys-558 had no effect on receptor phosphorylation, its substitution with proline produced high spontaneous receptor phosphorylation, suggesting that the predicted alpha-helical conformation is involved in the inhibition. A synthetic peptide comprising Tyr-553 through Ile-563 showed circular dichroism spectra characteristic of alpha-helix, supporting the structural prediction. Thus, the KIT intracellular juxtamembrane region contains important residues which, in a putative alpha-helical conformation, exert inhibitory control on the kinase activity of ligand-unoccupied receptor.
CC Enzymes - Chemical and physical 10806
Biochemistry methods - Proteins, peptides and amino acids 10054
Biophysics - Methods and techniques 10504
Biophysics - Molecular properties and macromolecules 10506
General biology - Miscellaneous 00532
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques

IT Chemicals & Biochemicals
KIT receptor kinase: intracellular juxtamembrane region
IT Methods & Equipment
circular dichroism: analytical method, spectroscopic techniques: CB, spectroscopic techniques: CT; immunoblotting: Analysis/Characterization Techniques: CB, analytical method; immunoprecipitation: isolation method, precipitation techniques; site-directed mutagenesis: analytical method, mutagenesis, protein engineering; transfection: gene expression/vector techniques, genetic method
IT Miscellaneous Descriptors
amino acid substitution; spontaneous receptor phosphorylation: inhibition
ORGN Classifier
Cercopithecidae 86205
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
COS cell line
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman Vertebrates, Nonhuman Primates, Primates, Vertebrates
RN 9031-44-1 (KINASE)

L119 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:229797 BIOSIS
DN PREV199900229797
TI Transgenic mice expressing **stem cell factor** in basal keratinocytes develop postinflammatory hyperpigmentation in response to irritant and allergic contactants.
AU Carter, E. L. [Reprint author]; Tigelaar, R. E.; **Longley, B. J.**
CS Department of Dermatology, Columbia University, New York, NY, USA
SO Journal of Investigative Dermatology, (April, 1999) Vol. 112, No. 4, pp. 539. print.
Meeting Info.: 60th Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA. May 5-9, 1999.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999
CC Integumentary system - General and methods 18501
Cytology - Animal 02506
Biochemistry studies - General 10060
Blood - General and methods 15001
Immunology - General and methods 34502
Allergy 35500
Toxicology - General and methods 22501
Endocrine - General 17002
General biology - Symposia, transactions and proceedings 00520
IT Major Concepts
Allergy (Clinical Immunology, Human Medicine, Medical Sciences); Dermatology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
basal keratinocyte: integumentary system; epidermis: integumentary system
IT Diseases
postinflammatory hyperpigmentation: integumentary system disease
IT Chemicals & Biochemicals
allergic contactant: allergen; irritant contactant: toxin; keratin 14 promoter; **stem cell factor**: expression
IT Miscellaneous Descriptors
Meeting Abstract

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: model, transgenic
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L119 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:304050 BIOSIS
DN PREV199800304050
TI Murine cutaneous mastocytosis and epidermal melanocytosis induced by keratinocyte expression of transgenic **stem cell factor.**
AU Kunisada, Takahiro [Reprint author]; Lu, Shu-Zhuang; Yoshida, Hisahiro; Nishikawa, Satomi; Nishikawa, Shin-Ichi; Mizoguchi, Masako; Hayashi, Shin-Ichi; Tyrrell, Lynda; Williams, David A.; Wang, Xiaomei; **Longley, B. Jack** [Reprint author]
CS Sect. Dermatopathol., Coll. Physicians Surg. Columbia Univ., 630 W. 168th St., VC 5-578, New York, NY 10032, USA
SO Journal of Experimental Medicine, (May 18, 1998) Vol. 187, No. 10, pp. 1565-1573. print.
CODEN: JEMEAV. ISSN: 0022-1007.
DT Article
LA English
ED Entered STN: 15 Jul 1998
Last Updated on STN: 15 Jul 1998
AB The growth and differentiation of mast cells and melanocytes require **stem cell factor (SCF)**, the ligand for the kit receptor tyrosine kinase. **SCF** may exist as a membrane-bound or soluble molecule. Abnormalities of the **SCF** -kit signaling pathway, with increased local concentrations of soluble **SCF**, have been implicated in the pathogenesis of the human disease cutaneous mastocytosis, but have not yet been shown to play a causal role. To investigate both the potential of **SCF** to cause mastocytosis and its role in epidermal melanocyte homeostasis, we targeted the expression of **SCF** to epidermal keratinocytes in mice with two different transgenes controlled by the human keratin 14 promoter. The transgenes contained cDNAs that either produced **SCF**, which can exist in both membrane-bound and soluble forms, or **SCF**, which remains essentially membrane bound. Murine epidermal keratinocyte expression of membrane-bound/ soluble **SCF** reproduced the phenotype of human cutaneous mastocytosis, with dermal mast cell infiltrates and epidermal hyperpigmentation, and caused the maintenance of a population of melanocytes in the interadnexal epidermis, an area where melanocytes and melanin are found in human skin but where they are not typically found in murine skin. Expression of membrane-bound **SCF** alone resulted in epidermal melanocytosis and melanin production, but did not by itself cause mastocytosis. We conclude, first, that a phenotype matching that of human mastocytosis can be produced in mice by keratinocyte overproduction of soluble **SCF**, suggesting a potential cause of this disease. Second, we conclude that keratinocyte expression of membrane-bound **SCF** results in the postnatal maintenance of epidermal melanocytes in mice. Since the resulting animals have skin that more closely approximates human skin than do normal mice, their study may be more relevant to human melanocyte biology than the study of skin of normal mice.
CC Integumentary system - General and methods 18501
Genetics - Animal 03506
Biochemistry studies - General 10060
IT Major Concepts

Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
interadnexal epidermis: integumentary system; keratinocyte: integumentary system; mast cell: immune system
IT Diseases
cutaneous mastocytosis: congenital disease, integumentary system disease
Mastocytosis (MeSH)
IT Diseases
epidermal melanocytosis: integumentary system disease
IT Chemicals & Biochemicals
melanin; transgenic **stem cell factor**: expression
IT Miscellaneous Descriptors
melanocyte development
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: transgenic
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L119 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:122069 BIOSIS
DN PREV199800122069
TI **SCF** and c-kit in mastocytosis. A Pandora's box holding more theories than proven facts (and reply).
AU Henz, Beate M. [Reprint author]; **Longley, B. Jack**
CS Dep. Dermatol., Free Univ. Berlin, Rudolf Virchow Hosp., Berlin, Germany
SO Journal of Investigative Dermatology, (Feb., 1998) Vol. 110, No. 2, pp. 186-187. print.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Letter
LA English
ED Entered STN: 5 Mar 1998
Last Updated on STN: 5 Mar 1998
CC Integumentary system - General and methods 18501
Endocrine - General 17002
Pediatrics - 25000
Development and Embryology - General and descriptive 25502
IT Major Concepts
Integumentary System (Chemical Coordination and Homeostasis)
IT Diseases
mastocytosis: congenital disease, integumentary system disease
Mastocytosis (MeSH)
IT Chemicals & Biochemicals
c-kit: mutation; stem cell growth factor
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: child
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L119 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:434032 BIOSIS
DN PREV199799733235
TI Chymase cleavage of **stem cell factor** yields

a bioactive, soluble product.
AU **Longley, B. Jack** [Reprint author]; Tyrrell, Lynda; Ma, Yongsheng; Williams, David A.; Halaban, Ruth; Langley, Keith; Lu, Hsieng S.; Schechter, Norman M.
CS Sect. Dermatopathol., Coll. Physicians Surgeons Columbia Univ., 630 West 168th St., VC5-578, New York, NY 10032, USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 17, pp. 9017-9021.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 8 Oct 1997
Last Updated on STN: 8 Oct 1997
AB **Stem cell factor** (**SCF**) is produced by stromal cells as a membrane-bound molecule, which may be proteolytically cleaved at a site close to the membrane to produce a soluble bioactive form. The proteases producing this cleavage are unknown. In this study, we demonstrate that human mast cell chymase, a chymotrypsin-like protease, cleaves **SCF** at a novel site. Cleavage is at the peptide bond between Phe-158 and Met-159, which are encoded by exon 6 of the **SCF** gene. This cleavage results in a soluble bioactive product that is 7 amino acids shorter at the C terminus than previously identified soluble **SCF**. This research shows the identification of a physiologically relevant enzyme that specifically cleaves **SCF**. Because mast cells express the KIT protein. the receptor for **SCF**, and respond to **SCF** by proliferation and degranulation, this observation identifies a possible feedback loop in which chymase released from mast cell secretory granules may solubilize **SCF** bound to the membrane of surrounding stromal cells. The liberated soluble **SCF** may in turn stimulate mast cell proliferation and differentiated functions; this loop could contribute to abnormal accumulations of mast cells in the skin and hyperpigmentation at sites of chronic cutaneous inflammation.
CC Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - Physiological studies 10808
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics)
IT Chemicals & Biochemicals
CHYMASE
IT Miscellaneous Descriptors
ACTIVITY; CHYMASE; CLEAVAGE; ENZYME SUBSTRATE; ENZYMOLOGY; MAST CELL ENZYME; MEMBRANE MOLECULE; SOLUBLE BIOACTIVE FORM; **STEM CELL FACTOR**; STOMAL CELL POLYPEPTIDE
RN 97501-92-3 (CHYMASE)

L119 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:345950 BIOSIS
DN PREV199799645153
TI Human skin/SCID mouse chimeras an an in vivo model for human cutaneous mast cell hyperplasia.
AU Christofidou-Solomidou, Melpo; **Longley, B. Jack**; Whitaker-Menezes, Diana; Albelda, Steven M.; Murphy, George F. [Reprint author]
CS Jefferson Alumni Hall, Suite 545, 1020 Locust St., Philadelphia, PA 19107-6799, USA
SO Journal of Investigative Dermatology, (1997) Vol. 109, No. 1, pp. 102-107.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Article
LA English
ED Entered STN: 11 Aug 1997
Last Updated on STN: 11 Aug 1997
AB Human skin xenografted to mice with severe combined immunodeficiency

syndrome (SCID) was evaluated to determine the integrity and fate of human dermal mast cells. There was an approximately 3-fold increase in number of dermal mast cells by 3 mo after engraftment (p lt 0.05). These cells were responsive to conventional mast cell secretagogues and were confirmed to be of human origin by ultrastructural characterization of granule substructure and by reactivity for the human mast cell proteinase, chymase. CD1a+ Langerhans cells, also bone marrow-derived cells, failed to show evidence of concomitant hyperplasia, and increased mast cell number was not associated with alterations in number of dermal vascular profiles identified immunohistochemically for human CD31. RT-PCR analysis demonstrated human but not murine **stem cell factor** (**SCF**; also termed mast cell growth factor, c-kit ligand) mRNA in xenografts. Epidermal reactivity for **stem cell factor** protein shifted from a cytoplasmic pattern to an intercellular pattern by 3 mo after engraftment, suggesting a secretory phenotype, as previously documented for human cutaneous mastocytosis. The majority (gt 90%) of mast cells demonstrated membrane reactivity for human **SCF** at the time points of peak hyperplasia. These data establish SCID mouse recipients of human skin xenografts as a potential in vivo model for cutaneous mast cell hyperplasia.

CC Cytology - Animal 02506
Cytology - Human 02508
Anatomy and Histology - Regeneration and transplantation 11107
Blood - General and methods 15001
Endocrine - General 17002
Integumentary system - General and methods 18501

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Integumentary System (Chemical Coordination and Homeostasis); Physiology

IT Miscellaneous Descriptors
CONGENITAL DISEASE; CUTANEOUS MAST CELL HYPERPLASIA; CUTANEOUS MASTOCYTOSIS; DERMAL MAST CELL; HUMAN SKIN XENOGRAFT; IMMUNE SYSTEM; INTEGUMENTARY SYSTEM; INTEGUMENTARY SYSTEM DISEASE; MESSENGER RNA; MRNA; SCID MOUSE; SEVERE COMBINED IMMUNODEFICIENCY MOUSE; **STEM CELL FACTOR**

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Muridae
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

=> s l116 not l119
L121 7 L116 NOT L119

=> d all tot

L121 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2004:255424 BIOSIS
DN PREV200400254772

TI Autoimmune cutaneous hypopigmentation following DNA vaccination with TRP-2 in **SCF** transgenic mice: Mimicking vitiligo in humans.
AU Trcka, J. [Reprint Author]; Engelhorn, M.; Schaed, S. G. [Reprint Author]; Carter, E.; Broecker, E. B. [Reprint Author]; **Longley, B. J.**; Houghton, A. N.
CS Univ.-Hautklinik, 97080, Wuerzburg, Germany
SO Archives of Dermatological Research, (February 2004) Vol. 295, No. 8-9, pp. 382. print.
Meeting Info.: 31st Annual Meeting of the Arbeitsgemeinschaft Dermatologische Forschung in cooperation with the Deutsche Dermatologische Gesellschaft. Berlin, Germany. February 26-28, 2004.
ISSN: 0340-3696 (ISSN print).
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 12 May 2004
Last Updated on STN: 12 May 2004
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
epidermal keratinocyte: integumentary system; melanocyte: integumentary system; skin: integumentary system
IT Diseases
autoimmune cutaneous hypopigmentation: immune system disease; integumentary system disease
IT Diseases
vitiligo: integumentary system disease
Vitiligo (MeSH)
IT Chemicals & Biochemicals
cytokeratin 14: promoter activity; tyrosinase related protein-2 [TRP-2]
IT Methods & Equipment
DNA vaccination: genetic techniques, laboratory techniques; immunization: clinical techniques, therapeutic and prophylactic techniques
IT Miscellaneous Descriptors
tumor immunity
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
C57/BL6 mouse (common): transgenic
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
GEN mouse **SCF** gene [mouse **stem cell factor** gene] (Muridae): transgene

L121 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2004:188195 BIOSIS
DN PREV200400184749
TI A role for **SCF**/c-kit signaling in the morphogenesis and cyclic regeneration of hair pigmentation unit.
AU Botchkareva, N. V. [Reprint Author]; Botchkarev, V. A. [Reprint Author]; Khlgatian, M. [Reprint Author]; Sharov, A. A. [Reprint Author];

Longley, B. J.; Gilchrest, B. A. [Reprint Author]
CS Dept. of Dermatology, Boston University School of Medicine, Boston, USA
SO Journal of Investigative Dermatology Symposium Proceedings, (June 2003) Vol. 8, No. 1, pp. 128. print.
Meeting Info.: Third Intercontinental Meeting of Hair Research Societies. Tokyo, Japan. June 13-15, 2001.
ISSN: 1087-0024 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802
Integumentary system - Physiology and biochemistry 18504
IT Major Concepts
Biochemistry and Molecular Biophysics; Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
hair: integumentary system; hair follicle: integumentary system; keratinocytes: integumentary system; melanocyte: integumentary system
IT Chemicals & Biochemicals
SCF/c-kit: signaling; c-kit; c-kit receptor; melanogenic proteins; tyrosinase [EC 1.14.18.1]
IT Methods & Equipment
double immunofluorescence: immunologic techniques, laboratory techniques; multi-color confocal microscopy: imaging and microscopy techniques, laboratory techniques
IT Miscellaneous Descriptors
morphogenesis
RN 9002-10-2 (tyrosinase)
9002-10-2 (EC 1.14.18.1)

L121 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:435404 BIOSIS
DN PREV200300435404
TI Effects of tyrosine kinase inhibitor STI571 on human mast cells bearing wild-type or mutated c-kit.
AU Akin, Cem [Reprint Author]; Brockow, Knut; D'Ambrosio, Claudio; Kirshenbaum, Arnold S.; Ma, Yongsheng; **Longley, B. Jack**; Metcalfe, Dean D.
CS Laboratory of Allergic Diseases, NIAID/NIH, 10 Center Drive, Building 10, Room 11C205, MSC 1881, Bethesda, MD, 20892-1881, USA
cakin@niaid.nih.gov
SO Experimental Hematology (New York), (August 2003) Vol. 31, No. 8, pp. 686-692. print.
ISSN: 0301-472X (ISSN print).
DT Article
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003
AB Objective: STI571 is a tyrosine kinase inhibitor which inhibits the kinase activity of kit, the receptor for **stem cell factor** (**SCF**). Because activating mutations of c-kit affecting codon 816 are associated with human mast cell neoplasms, we determined whether STI571 exerted a similar cytotoxic effect on neoplastic and normal human mast cells. Methods: We investigated the effect of addition of STI571 in increasing concentrations (0.01 to 10 micromolar) to two HMC-1 human mast cell leukemia cell lines carrying two different activating c-kit mutations in codons 816 or 560, as well as the effect of the drug on short-term bone marrow cultures obtained from patients who

carry a mutated codon 816 or wild-type c-kit. Results: STI571 failed to inhibit the growth of HMC-1560,816 cells bearing a codon 816 mutation but effectively suppressed the proliferation of HMC-1560 carrying c-kit with the wild-type codon 816. STI571 did not induce preferential killing of neoplastic bone marrow mast cells in short-term cultures from patients bearing a codon 816 c-kit mutation. In contrast, STI571 caused a dramatic reduction in mast cells in patients without codon 816 c-kit mutations. Conclusion: These results suggest that STI571, while effectively killing mast cells with wild-type c-kit, did not show preferential cytotoxicity to neoplastic human mast cells and thus may not be effective in the treatment of human systemic mastocytosis associated with codon 816 c-kit mutations.

CC Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Integumentary system - Pathology 18506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Immunology 24003
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Neoplasms - Blood and reticuloendothelial neoplasms 24010
Gerontology 24500
Pediatrics 25000
Development and Embryology - Pathology 25503
Tissue culture, apparatus, methods and media 32500
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology

IT Parts, Structures, & Systems of Organisms
bone marrow: blood and lymphatics, immune system; mast cells: immune system

IT Diseases
mast cell leukemia: blood and lymphatic disease, immune system disease, neoplastic disease
Leukemia, Mast-Cell (MeSH)

IT Diseases
systemic mastocytosis: congenital disease, integumentary system disease

IT Chemicals & Biochemicals
STI571: antineoplastic-drug, enzyme inhibitor-drug; c-kit: mutation; **stem cell factor [SCF]**; tyrosine kinase [EC 2.7.1.112]: regulation

IT Methods & Equipment
short-term culture: culturing techniques, laboratory techniques

IT Miscellaneous Descriptors
tumor growth regulation

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HMC-1 cell line (cell line): human mast cell leukemia cells
K562 cell line (cell line): human chronic myeloid leukemia cells
human (common): adolescent, adult, aged, middle age, patient, female, male
Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 152459-95-5 (STI571)
80449-02-1 (tyrosine kinase)
80449-02-1 (EC 2.7.1.112)

L121 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:483580 BIOSIS
DN PREV200100483580
TI The C-kit signaling pathways in normal and mastocytosis mast cells.
AU Chan, I. [Reprint author]; Kayashima, K. [Reprint author]; Ma, Y.; **Longley, B.**; Tharp, M. [Reprint author]
CS Dermatology, Rush-Presbyterian-St-Luke's Medical Center, Chicago, IL, USA
SO Journal of Investigative Dermatology, (August, 2001) Vol. 117, No. 2, pp. 489. print.
Meeting Info.: 62nd Annual Meeting of the Society for Investigative Dermatology. Washington, DC, USA. May 09-12, 2001.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Oct 2001
Last Updated on STN: 23 Feb 2002
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
Development and Embryology - Pathology 25503
Immunology - General and methods 34502
IT Major Concepts
Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
mast cell: immune system; skin: integumentary system
IT Diseases
mastocytosis: congenital disease, integumentary system disease
Mastocytosis (MeSH)
IT Chemicals & Biochemicals
C-kit: signaling pathways; C-kit receptor; JAK-3; Janus kinases; UO126; WHI-P131; mitogen activated kinases; **stem cell factor**
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HMC-1 cell line: human mastocytosis cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 161384-16-3 (Janus kinases)
202475-60-3 (WHI-P131)

L121 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:320160 BIOSIS
DN PREV200100320160
TI Effects of the tyrosine-kinase inhibitor STI571 on mutated kit and neoplastic mast cells.
AU Akin, Cem [Reprint author]; **Longley, B. Jack**; Brockow, Knut [Reprint author]; Metcalfe, Dean D. [Reprint author]
CS Laboratory of Allergic Diseases, NIAID, NIH, Bethesda, MD, USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 747a. print.

Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
AB STI571 is a tyrosine kinase inhibitor which inhibits bcr-abl, and the kinase activity of the receptor for PDGF; and has been reported to inhibit **stem cell factor** receptor (KIT) and tumors bearing activating KIT mutations. It has been shown to have cytotoxic activity on chronic myeloid leukemia (CML) cells carrying bcr-abl and is currently under evaluation as a treatment for CML. Because activating mutations of c-kit affecting codon 816 are associated with most adult human mast cell neoplasms, we determined whether STI 571 exerted a similar cytotoxic effect on neoplastic human mast cells. We thus investigated the effect of addition of STI571 in increasing concentrations (0.01 to 10 micromolar) to bcr-abl positive (K562) and negative (U937) cells as well as the HMC-1 human mast cell leukemia cell line carrying two different activating c-kit mutations in codons 816 or 560. STI571 failed to inhibit the growth of U937 cells as well as HMC-1 cells bearing the 816 mutation but effectively suppressed the proliferation of K562 cells and HMC-1 expressing only the 560 mutation at concentrations greater than 0.1 micromolar. Consistent with these in vitro observations, STI571 inhibited ligand induced phosphorylation of transiently transfected wild type KIT in COS cells but failed to inhibit KIT activated by the 816 mutation in the same system. We then determined the effects of STI571 on mast cell numbers in bone marrow aspirates obtained from 7 patients with mastocytosis. The bone marrow mononuclear cell fractions containing the mast cells were incubated in increasing concentrations of STI571 for up to 8 days in serum-free medium in presence of **stem cell factor.** STI571 caused a dose-dependent reduction in total cell numbers as well as absolute mast cell numbers; however STI571 did not induce preferential killing of neoplastic mast cells under these culture conditions. These results suggest that STI571 does not significantly inhibit autophosphorylation of KIT carrying an activating codon 816 mutation at pharmacologic doses and is not preferentially cytotoxic to neoplastic human mast cells in short term cultures. Studies evaluating the effects of STI571 on long-term human mast cell cultures are currently underway.
CC Neoplasms - Therapeutic agents and therapy 24008
General biology - Symposia, transactions and proceedings 00520
Cytology - Human 02508
Genetics - General 03502
Genetics - Human 03508
Pathology - Therapy 12512
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
STI 571: antineoplastic-drug, mutated KIT **stem cell factor** receptor effects, tyrosine kinase inhibitor
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Classifier
Hominidae 86215
Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HMC-1 cell line: drug treatment, human mast cell leukemia cell line, in-vitro model system
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 152459-95-5 (STI 571)

L121 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:231346 BIOSIS
DN PREV200100231346
TI **SCF**/c-kit signaling is required for cyclic regeneration of the hair pigmentation unit.
AU Botchkareva, Natalia V.; Khlgatian, Mary; **Longley, B. Jack**; Botchkarev, Vladimir A.; Gilchrest, Barbara A. [Reprint author]
CS Department of Dermatology, Boston University School of Medicine, 609 Albany St., Boston, MA, 02118, USA
bgilchre@bu.edu
SO FASEB Journal, (March, 2001) Vol. 15, No. 3, pp. 645-658. print.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Article
LA English
ED Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002
AB Hair graying, an age-associated process of unknown etiology, is characterized by a reduced number and activity of hair follicle (HF) melanocytes. **Stem cell factor** (**SCF**) and its receptor c-kit are important for melanocyte survival during development, and mutations in these genes result in unpigmented hairs. Here we show that during cyclic HF regeneration in C57BL/6 mice, proliferating, differentiating, and melanin-producing melanocytes express c-kit, whereas presumptive melanocyte precursors do not. **SCF** overexpression in HF epithelium significantly increases the number and proliferative activity of melanocytes. During the induced hair cycle in C57BL/6 mice, administration of anti-c-kit antibody dose-dependently decreases hair pigmentation and leads to partially depigmented (gray) or fully depigmented (white) hairs, associated with significant decreases in melanocyte proliferation and differentiation, as determined by immunostaining and confocal microscopy. However, in the next hair cycle, the previously treated animal grow fully pigmented hairs with the normal number and distribution of melanocytes. This suggests that melanocyte stem cells are not dependent on **SCF**/c-kit and when appropriately stimulated can generate melanogenically active melanocytes. Therefore, the blockade of c-kit signaling offers a fully reversible model for hair depigmentation, which might be used for the studies of hair pigmentation disorders.
CC Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Integumentary system - Physiology and biochemistry 18504
IT Major Concepts
Biochemistry and Molecular Biophysics; Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
hair: integumentary system, graying, pigmentation unit; pigmentation unit, cyclic regeneration
IT Chemicals & Biochemicals
c-kit; **stem cell factor**
IT Miscellaneous Descriptors
signal transduction
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name
mouse: strain-C57BL/6
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L121 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:389499 BIOSIS
DN PREV200000389499
TI Indolinone derivatives inhibit constitutively activated KIT mutants and kill neoplastic mast cells.
AU Ma, Yongsheng; Carter, Eric; Wang, Xiaomei; Shu, Chang; McMahon, Gerald; **Longley, B. Jack** [Reprint author]
CS Department of Dermatology, Section of Dermatopathology, College of Physicians and Surgeons, Columbia University, 630 West 168th Street, Vanderbilt Clinic 15-221, New York, NY, 10032, USA
SO Journal of Investigative Dermatology, (February, 2000) Vol. 114, No. 2, pp. 392-394. print.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Article
LA English
ED Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002
AB Mastocytosis is a neoplastic disease caused at least in part by somatic mutations of the c-KIT protooncogene resulting in constitutive activation of its protein product, KIT, the receptor tyrosine kinase for **stem cell factor.** KIT stimulates mast cell proliferation and prevents apoptosis of neoplastic mast cells. To develop potential therapies for mastocytosis we used indolinones, small molecules that inhibit tyrosine kinases. Four indolinone derivatives (SU4984, SU6663, SU6577, and SU5614) inhibited wild-type KIT, but variably inhibited constitutively activated KIT mutants. SU4984, SU6577, and SU5614 were effective against KIT with juxtamembrane activating mutations, whereas only SU6577 could suppress KIT containing either juxtamembrane or kinase domain activating mutations. Furthermore, SU4984, SU6577, and SU5614 killed neoplastic mast cells expressing a juxtamembrane-mutated KIT, whereas SU4984 and SU6577 killed neoplastic mast cells expressing KIT bearing a kinase domain mutation. These data show a direct correlation between inhibition of constitutively activated KIT and the death of neoplastic mast cells, and point to specific tyrosine kinase inhibitors as a potential therapy aimed directly at a cause of mastocytosis.
CC Development and Embryology - Pathology 25503
Cytology - Animal 02506
Genetics - General 03502
Genetics - Animal 03506
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
Neoplasms - Immunology 24003
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Integumentary System (Chemical Coordination and Homeostasis); Tumor Biology
IT Diseases
mastocytosis: congenital disease, integumentary system disease
Mastocytosis (MeSH)
IT Chemicals & Biochemicals
indolinone derivatives; **stem cell factor;**
tyrosine kinase; murine c-KIT gene: mutation

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ORGN Classifier
        Muridae   86375
     Super Taxa
        Rodentia; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        P815 cell line: neoplastic mast cells
     Taxa Notes
        Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
        Rodents, Vertebrates
RN   80449-02-1 (tyrosine kinase)


=> d his


     (FILE 'HOME' ENTERED AT 16:31:55 ON 12 AUG 2004)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 16:32:04 ON 12 AUG 2004
               E LONGLEY B/AU
L1           33 S E4-E6
L2           11 S E42
L3            7 S E37
L4            1 S E36
L5           52 S L1-L4
L6          414 S STEM CELL (L) FACTOR (L) SIGNAL? (L) PATHWAY
L7            3 S L5 AND L6
               E STEM CELL FACTOR/CT
L8         2301 S E3
               E E3+ALL
L9         1126 S E5,E6
L10        3427 S L8,L9
L11          20 S L10 (L) SIGNAL? PATHWAY
L12         208 S L10 AND SIGNAL?(L)PATHWAY?
L13         102 S L10 AND SIGNAL? PATHWAY?
L14         494 S L6,L11-L13
L15        2182 S L10 AND (PD<=19990506 OR PRD<=19990506 OR AD<=19990506)
               E CONTACT DERMATITIS/CT
               E E3+ALL
L16        3380 S E2
               E DERMATITIS/CT
L17        1494 S E5,E6,E12
               E E3+ALL
L18       11725 S E8+NT
L19        2277 S CONTACT DERMATITIS
L20           6 S L15 AND L16-L19
               E HYPERPIGMENTATION/CT
               E E3+ALL
L21         196 S E2
L22         570 S HYPERPIGMENT?
L23           8 S L15 AND L21,L22
               E ASTHMA/CT
L24       15205 S E3-E5
               E E3+ALL
L25       15205 S E9
               E E11+ALL
L26        8847 S E5,E6
L27       29150 S ?ASTHMA?
L28          15 S L15 AND L24-L27
               E SKIN INFLAMMATION/CT
               E E4+ALL
               E SKIN, DISEASE/CT
               E CUTANEOUS INFLAMMATION/CT
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                E SKIN DISEASE/CT
L29           1 S E4
                E E4+ALL
                E E2+ALL
L30       69482 S E6,E7,E5+NT
L31          37 S L15 AND L29,L30
L32          11 S L15 AND (SKIN OR DERM? OR EPIDERM? OR CUTAN?)(S)?INFLAM?
                E BRONCHOSPASM/CT
                E E3+ALL
L33           1 S L15 AND E2
L34           2 S L15 AND ?BRONCH?(L)?SPASM?
                E ANAPHYLAXIS/CT
L35           5 S L15 AND E3-E7
                E E3+ALL
L36           5 S L15 AND E3,E2+NT
L37          11 S L15 AND E16+OLD,NT
L38          49 S L15 AND E18+OLD,NT
L39          16 S L15 AND E19+OLD,NT
L40           0 S L15 AND E20+OLD,NT
                E MASTOCYTOSIS/CT
                E E3+ALL
L41         249 S E2
L42         356 S MASTOCYTOS?
L43          15 S L15 AND L41,L42
                E URTICARIA/CT
L44        1099 S E3+OLD,NT
L45        1885 S URTICAR?
L46           6 S L15 AND L44,L45
                E HYPERSENSITIVITY/CT
                E E3+ALL
L47           2 S L15 AND E2
L48           0 S L15 AND E6
L49           0 S L15 AND E8
L50           6 S L15 AND HYPERSENSITIV?
                E AIRWAY INFLAMMATION/CT
                E E3+ALL
L51           0 S L15 AND E2
                E RESPIRATORY TRACT, DISEASE/CT
L52          57 S L15 AND E3+OLD,NT
                E INTERSTITIAL CYSTITIS/CT
                E CYSTITIS/CT
L53           0 S L15 AND E3
                E E3+ALL
L54           0 S L15 AND E2
L55           0 S L15 AND INTERSTIT? CYSTIT?
L56         928 S L15 AND KIT
L57         177 S L56 AND (?TUMOR? OR ?NEOPLAS? OR ?MALIGN? OR ?CANCER? OR ?MET
                E CONTRACEPTION/CT
                E E7+ALL
L58           5 S L15 AND E5
                E E7+ALL
L59          53 S L15 AND E3+NT
L60         350 S L20,L23,L28,L31-L39,L43,L46,L47,L50,L52,L57-L59
L61          70 S L60 AND SIGNAL?
L62          25 S L61 AND PATHWAY
L63          24 S L60 AND L14
L64          25 S L62,L63
L65          25 S L7,L64
L66           6 S L65 AND (SKIN OR EPIDERM? OR DERM? OR CUTAN? OR SUBCUTAN?)
L67           3 S L66 AND L5
L68          19 S L65 NOT L66
                SEL DN AN 1 12 13
L69           3 S E1-E9
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L70             6 S L67,L69
                  E SIGNAL/CT
                  E E40+ALL
L71        111592 S E1
                  E E11+ALL
L72        309686 S E4+NT
L73            37 S L60 AND L71,L72
L74            21 S L73 NOT L65
                  SEL DN AN 4 5
L75             2 S E1-E6
                  SEL DN AN 21 L74
L76             1 S E7-E9
L77             9 S L70,L75,L76 AND L1-L76
L78             9 S L77 AND (SCF OR STEM CELL FACTOR)

     FILE 'HCAPLUS' ENTERED AT 17:02:34 ON 12 AUG 2004

     FILE 'WPIX' ENTERED AT 17:03:59 ON 12 AUG 2004
L79          1228 S (STEM CELL FACTOR OR SCF)/BIX
L80             3 S L79 AND CONTACT DERMATITIS/BIX
L81           122 S (B04-H16 OR C04-H16)/MC
L82             1 S L81 AND CONTACT DERMATITIS/BIX
L83            77 S L79,L81 AND (B14-N17? OR C14-N17? OR B12-A07 OR C12-A07)/MC
L84            24 S L79,L81 AND (B14-N17C OR C14-N17C)/MC
L85            24 S L80,L82,L84
                  E LONGLEY/AU
L86             3 S E7
L87             1 S L86 AND L79,L81
L88             2 S L86 NOT L87
L89             3 S L80,L82,L87
L90             3 S (B04-M01 OR C04-M01)/MC AND L85
L91             1 S L90 NOT JAMM
L92             6 S L85 AND SIGNAL?/BIX
L93             3 S L89 AND L79-L92

     FILE 'WPIX' ENTERED AT 17:14:46 ON 12 AUG 2004

     FILE 'DPCI' ENTERED AT 17:14:58 ON 12 AUG 2004
                  E LONGLEY/AU
L94             2 S E7

     FILE 'DPCI' ENTERED AT 17:15:35 ON 12 AUG 2004

     FILE 'MEDLINE' ENTERED AT 17:16:08 ON 12 AUG 2004
                  E STEM CELL FACTOR/CT
                  E E3+ALL
L95          2592 S E30
L96          1793 S L95 AND PY<=1999
                  E CONTACT DERMATITIS/CT
                  E E3+ALL
L97             0 S L96 AND E2+NT
L98             0 S L96 AND CONTACT DERMATITIS
                  E DERMATITIS/CT
                  E E3+ALL
L99            56 S L96 AND E3+NT
L100            0 S L99 AND E4+NT
                  E HYPERPIGMENTATION/CT
                  E ASTHMA/CT
                  E SKIN INFLAMMATION/CT
                  E INFLAMMATION/CT
                  E BRONCHOSPASM/CT
                  E E3+ALL
                  E ANAPHYLAXIS/CT
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                E MASTOCYTOSIS/CT
                E URTICARIA/CT
                E HYPERSENSITIVITY/CT
                E AIRWAY INFLAMMATION/CT
                E RESPIRATORY/CT
                E RESPIRATORY DISEASE/CT
                E RESPIRATORY TRACT DISEASE/CT
L101         49 S L96 AND (HYPERPIGMENTATION+NT OR ASTHMA+NT OR ANAPHYLAXIS+NT
                E BRONCHOSPASM/CT
                E E3+ALL
L102          0 S L96 AND E2+NT
                E INTERSTITIAL CYSTITIS/CT
                E E3+ALL
L103          1 S L96 AND E2+NT
L104        374 S L96 AND C4./CT
L105        402 S L99,L101,L104
L106         67 S L105 AND SIGNAL?
L107         27 S L106 AND PATHWAY?
                E SIGNAL/CT
                E E19+ALL
L108         27 S E2+NT AND L106
L109         27 S E2+NT AND L105
L110         40 S L107-L109
L111          2 S STEM CELL FACTOR(L)AI/CT AND L110
L112         12 S L110 AND INHIBIT?
L113          7 S L112 AND L95/MAJ
L114          2 S L111 AND L113

     FILE 'MEDLINE' ENTERED AT 17:26:21 ON 12 AUG 2004

     FILE 'BIOSIS' ENTERED AT 17:26:27 ON 12 AUG 2004
                E LONGLEY/AU
L115         44 S E8-E12
L116         14 S L115 AND (SCF OR STEM CELL FACTOR)
L117         30 S L115 NOT L116
L118         26 S L115 AND PY<=1999
L119          7 S L118 AND L116
L120         19 S L118 NOT L119

     FILE 'BIOSIS' ENTERED AT 17:28:38 ON 12 AUG 2004
L121          7 S L116 NOT L119

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